November 2014 - ISSUE 4

WKMJ

World Korean Medical Journal

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WKMJ
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FROM THE PUBLISHER

Welcome to the fourth issue of WKMJ!

In my role as the publisher of World Korean Medical Journal, I am blessed with numerous opportunities to meet and interact with some incredible people. Dr. Yung Man Lee of Sao Paulo, Brazil, who is featured in this issue, is a good example. I first met Dr. Lee on Feb 8, 2014 when I visited Sao Paulo to start the World Korean Medical Organization (WKMO)'s first regional forum. In this particular forum, Korean physicians from Korea, Europe, the United States, and South America gathered to discuss ethnic disparity of diseases in Latin America.

Dr. Yung Man Lee was one of the first Korean physicians to immigrate to Brazil. He came to Sao Paulo in 1966 and has practiced medicine since. His is a true family of physicians, totaling thirty physicians among his children and grandchildren, including his son Dr. Andre Lee, a professor of Surgery at Sao Paulo University Medical School, who also serves as a Board member in WKMO. Dr. Yung Man Lee's works as an immigrant physician and a community leader are inspiring, and they serve as legacies for our young generation.

WKMJ also introduces its new 'Medical Institute' section in this issue, where we featured the City of Hope (COH) National Medical Center. COH has a new model of Cancer Center, focused on innovative strategies to treat and prevent cancer. With sixteen Korean physicians as staff in COH, the hospital also aims to provide culturally competent care tailored to specifically Korean patients.

Thanks for reading. I wish you and your family Merry Christmas and Happy New Year!

Chul S. Hyun, MD, PhD
Publisher
President of WKMO
Weill Cornell Medical College

FROM THE EDITOR IN CHIEF

Dear Colleagues,

The Korean immigration to all corners of the world was a bold undertaking especially in the last half century. Korean Physicians immigrated elsewhere to seek new opportunities as well as opportunities not available in Korea at that time.

The early Korean physician immigrants in many countries had to navigate arduous and lengthy paths often having to retrain with a second residency to practice in the new countries. The early physician pioneers would help fellow physicians and this has happened in many countries. After a critical mass, local Korean physicians organized and met. As there are Korean heritage physician groups throughout the world, WKMO is trying to connect on global network.

The early Korean Physician pioneers like Dr. Yung Man Lee in Brazil is a success story featured in this issue. The regional WKMO forum in Brazil, largest country in South America, early this year was an opportunity to meet Dr. Lee and his son who gave us tour of Sao Palo University Hospital. The number of Korean medical students in Brazil is growing and some were able to attend the World Korean Medical Student Association (WKMSA) meeting in conjunction with the WKMO meeting in New York.

A new feature with this issue is a focus on a medical institution. City of Hope Hopsital in Duarte California right outside of LA is a comprehensive cancer center with a long history and a bright future. City of Hope has a number of Korean American physicians and forged a working relationship with MOU with Seoul National University thru interactions at the WKMO meetings. City of Hope recently recruited Dr. Larry Kwak from MD Anderson who is doing impressive cancer research

One of the major holidays in the U.S. is the Thanksgiving Holiday which originated from the early immigrants to the America surviving and making it. The spirit of the Thanksgiving holiday is especially pertinent to the Korean physicians that went abroad. We all should give thanks, and move forward in achieving goals. Happy Holidays and look forward to great 2015.

David Y. Ko, MD
Editor in Chief
Board Director of WKMO
Keck School of Medicine of USC

WKMJ RECAP OF SEPTEMBER ISSUE

WKMO Report
WKMO 3rd Annual Convention

On July 3-5, World Korean Medical Organization (WKMO) hosted its 3rd Annual Convention at Le Parker Meridien hotel in New York City. The convention focused on the theme of “Cultural Competence in Healthcare” and featured various programs focusing on issues of ethnic disparity in medical and surgical symposia. There were over 250 participants from 12 different countries.

Cover Story
Congressman Chung Ui-Hwa’s Journey from Medicine to the National Assembly

Dr. Chung Ui-Hwa was a neurosurgeon for 30 years. He was a well-known microvascular specialist. He started his political career as a healthcare expert member of New Korea Party. With his management principle of “profits made from patients will be used for patients”, Dr. Chung wanted to heal and make the society healthier as a politician-physician. Read our Issue 3 to find out more about Dr. Chung’s journey.

Entrepreneur Interview
The Global Medical Leadership of CEO, Kyoung-Ryul Lee

As a child, Kyoung-Ryul Lee felt more sadness than fear when he first encountered people with leprosy and disabled patients. As a physician, Dr. Lee believed that to ensure the health of an individual through medical prophylaxis before one becomes a patient is crucial. For such reason, Dr. Lee establishes Hanaro Medical Foundation to detect early and diagnose before people become seriously ill. Since then, Dr. Lee became a businessman to ensure people’s health globally. Read our Issue 3 to find out more about background story of Hanaro Medical Foundation.

Special Report I
Laboratory Payments to Referring Physicians

The mission of the HHS Office of Inspector General (OIG) is to protect the integrity of HHS programs as well as the health and welfare of program beneficiaries. Among other functions, OIG periodically issues Special Fraud Alerts to address what it perceives as industry-wide practices of concern to it, including what it deems to be trends in health care fraud, and to provide guidance to health care professionals and institutions on violations of Federal law, including the anti-kickback statute. Read our Issue 3 for more information about this special report.

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WKMO Report

1st Inaugural KUMA Conference

On November 15, 2014, celebrating its foundation, Korean UK Medical Association (KUMA) opened an anniversary conference for the first time at Sir Alexander Fleming Building, Imperial College London, UK.

a. Conference in process Imperial College London (Sir Alexander Fleming Building).

It was a one-day conference with inspiring and informative sessions which contained various topics including NHS healthcare system, lectures on procurement processes, working abroad, financial management tips, specialty applications, British Medical Association, etc. Opening statements were made by Dr. Hyunick Kim, the President of KUMA and many other significant individuals in healthcare industry from all across Europe including Professor Dae Kim, St. George's Hospital London, Professor Kei Cho, University of Bristol, Professor Andrew Levy, University of Bristol, Dr. Soo-Hyun Kim, St. George's, University of London, Dr. Yealin Chung, University of Bristol, Dr. Leehyok Woo, South Bucks CAMHS, Professor Colin Dayan, Cardiff University, Dr. Joonsoo Ha, KUMA, Dr. Hyunmi Park, KUMA Professional Development Officer, Dr. Johan Semby, Ophthalmologist from Sweden, Dr. Silvia Lee, Internal Medicine from Austria, Dr. David Kim, Urologist from Spain, Dr. Carol Moon from KUMA, and Dr. Elizabeth Lee from British Medical Association continued on providing great lectures.

b. Dr. Do Hyun Cho, W Medical Strategy Group and Dr. Chul Hyun, WKMO President at the KUMA Conference.

c. Starting from left, Deputy Director Seung Yeon Kim from Korea Ministry of Health and Welfare, Professor Kei Cho from Bristol University, Director Soo Woong Kim from KHIDI UK, and Researcher Eun Jong Jang from KHIDI UK.

WKMO supported the regional association KUMA as a sponsor. Dr. Chul S. Hyun, WKMO president, attended the event and presented a talk entitled 'WKMO: Mission and Goals'. He discussed the role of WKMO in establishing global network for Korean physicians. He also spoke about the upcoming WKMO Europe Forum to be held in London on March 21, 2015.

About 100 people from medical institutions, research institutions and universities attended this event and discussed about UK healthcare system and ways to draw up a plan to enhance network in order for global cooperation. According to KUMA, there are about 100 Korean physicians in UK, and this number is expected to grow as there is an increasing number of Korean medical students. Hence this conference was truly an epic event in the history of Korean-UK community.

The conference was followed by a Gala Dinner at Savora Rembrant Hotel where all the attendees came to celebrate the first KUMA Conference. During the gala, Dr. Chul S. Hyun delivered a special award to Dr. Hyunick Kim, President of KUMA in recognition of KUMA's service and commitment to WKMO.
Both events were sponsored by WKMO and KHIDI-UK.

d. Appreciation award to KUMA President Dr. Hyunick Kim from WKMO President Dr. Chul Hyun.

e. Congratulatory message of WKMO President Dr. Chul Hyun while Gala Dinner at Savora Rembrant Hotel.

INSPIRATIONAL KOREAN HEALTHCARE LEADER

"1st Korean Physician in Brazil, Pioneer Story of Dr. Yung Man Lee"

Dr. Lee on right receiving 'Honorary Sao Paulo Citizenship Award' in Aug 31, 2006.

1. Dr. Lee, you are famous for being the first Korean physician in Brazil. What was your motivation for becoming a physician, especially in another country, Brazil? Could you share your journey to become a doctor in Brazil, including any obstacles you may have encountered?

- Around 100 brave Koreans landed on Brazil in 1962 after government of Korea passed a law on overseas immigration. As Korea was still in recovery phase from postwar period, this law encouraged people of Korea to explore a new life abroad. After I obtained my MD from Busan Medical School, I decided to immigrate to Brazil. In 1965, my family got on the ship heading to the Port of Santos, Brazil. After seemingly endless days of sailing, we finally landed in Sao Paulo. Among numerous difficulties and challenges I had to face, first frustration came from the language barrier. In fact, I had never learned or even heard of Portuguese before I came to Brazil. Of course, my Korean medical license was useless here, and the language barrier prohibited me from even trying any other business. It took months of agony to decide whether to stay in Brazil or go back to Korea. I finally decided to stay and learn Portuguese, and this was how my immigrant life began.

I had to go through a revalidation process in order to prove my education. To achieve medical license in Brazil, I had to take exams that tested the education level of achievement in a range from middle school to college level in Brazil. The middle and high school level examination included history, geography and Portuguese subjects. Without any delays, I went directly to the middle school nearby and spoke to the school authority about my situation and got permission to study with the students. As I finished middle school level exams, again, I went directly to the high school nearby and study with the students. I studied as hard as I could and passed all the exams after all.

After achieving the three certificates of each subject, I had to look for a medical school, which will accept my application. Other than the three certificates, I had to submit a diploma, transcripts and medical license from Korea. I wrote to Korea and prepared for all the documentations. There I was well prepared and visited a medical school in Recife, Brazil. Professors discussed this special case and thankfully accepted my application.

The first Korean Medical Association Meeting in October, 1998. Dr.Jai Man Lee(brother) sitting in fifth of the bottom row was the first president. Dr. Yung Man Lee, sitting in second of the bottom row founded the association.

2. We have heard many stories about your free clinic and community medical volunteering services for those who needed medical attention but could not afford to see a doctor. What was your motivation and driving force to offer these kinds of activities?

- As soon as I got my medical license, I opened my first clinic named 'Yung Man Lee Clinic' in Korea town located in Sao Paulo. In the early period of immigration, many Korean immigrants could not have access to local hospitals especially due to the language barrier and cost. Koreans living near São Paulo poured into my office. The office door was usually opened until 2-3 AM. I offered free clinics for those who couldn't afford it to pay. I often visited shantytowns to treat both local patients and Korean immigrants. I never neglected those who could not receive proper medical treatment because of the cost.

Dr. Lee and Mrs. Lee at 'Honorary Sao Paulo Citizenship Award' ceremony.

At that time, illegal residents and people from low socioeconomic class were very common. I guess I didn't have the gut to ignore those who needed me as a physician. After awhile, I got used to seeing patients until 2-3 AM. Even though it was challenging, my heart was warm with happiness and satisfaction to help people in need with my talent.

Dr. Jai Man Lee(brother)'s family. Jai Man, Kim(sister in law) and Felix Lee(nephew).

3. In 2006, you've received an 'Honorary Sao Paulo Citizenship Award'. How did you feel about the award?

- It was such a huge honor to receive 'Honorary Sao Paulo Citizenship Award' in 2006. I honestly did not expect it at all which was a flattering surprise. I always thank the society for acknowledging and giving me over 15 awards and appreciation plaques for the works I enjoyed. On the other hand, a heavy responsibility fell on my shoulders.

Dr. Yung Man Lee, Ryun Hee Song (wife), sons (André Lee, Francisco Lee), daughter (Eliana Lee), grand sons (Victor, Lucas, Alexandre, Henrique e Guilherme) and daughters in law (Kyung and Selma).

4. How have Korean immigrants contributed to medical development in Brazil and how do you expect its future?

- There are many second-generation Korean immigrants who are working in medical field currently in Brazil. Three generations in my own family is now serving medical treatments as doctors. I have a strong belief that there will be ever more Korean doctors who can contribute both to Korean and Brazilian societies. Koreans always show high education fever. I personally believe that people have to learn wherever they are. Education is the key for future generation. Therefore, learning should be the first, second and third priority among others.

5. We understand that you have around 30 family members who are also currently practicing physicians including your son Dr. Dong Won Lee who is WKMO active member. You are probably a great influence and role model to them. Do you have any special educational viewpoints towards your descendants?

- I have three children. Both of my sons are physicians and my daughter is a dentist. Two of my grandchildren are also doing great at medical school getting prepared to become physicians. I think, though we live in different nations, it is important to learn our mother language and be able to at least know how to write a letter (in Korean) to parents and families in Korea.

6. You are one of the most significant pioneers of globalization of Korean medicine and WKMO members. Can you give them any advices?

- Within a global medical organization as WKMO, I believe we can promote goodwill together and be good strength to each other through various ways of interaction. Thank you. W

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Entrepreneur Interview

Scott J. Smith, Chairman of the Board and CEO,
Socrates Health Solutions

1. We understand that Socrates is a rapidly growing innovating medical technology company, and we admire the efficient and proactive expansion of Socrates. What are the major business philosophies or strategies of Socrates?

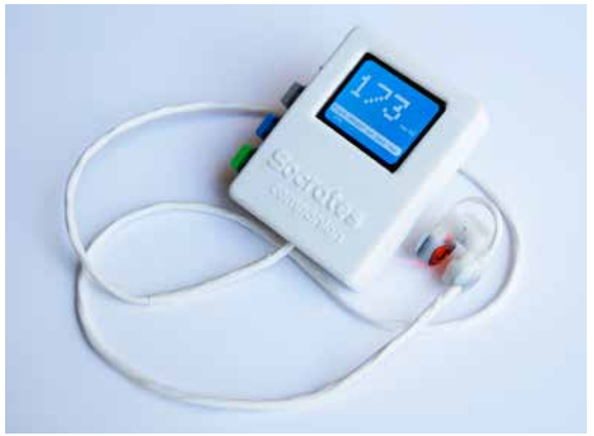
Socrates Health Solutions (Socrates), headquartered in Dallas, Texas, is a company committed to improving access to affordable care through the application of innovative technology and delivery models. Socrates is delivering an innovative diabetic monitoring experience through painless, accurate and truly non-invasive blood glucose monitoring device, Socrates Companion™. Consumers will be able to get accurate, pain-free readings for a fraction of the cost they are paying today when using traditional testing methods.

Our team is acutely focused on being authentic, straightforward, honest, creative and delivering results. This unique group of professionals is made up of senior healthcare professionals, scientists and physicians with over 150 combined years of experience. Collectively the team has brought twenty-three health care products from concept to commercialization.

Collectively, we recognize the global market opportunity for serving individuals with diabetes: worldwide there are 371 million diabetics. In the U.S. alone, there are currently 26 million diagnosed diabetics, 15 million undiagnosed diabetics, and another 79 million people in a pre-diabetic state where their blood sugar levels are higher than

normal. Close to 2 million people in the U.S. were newly diagnosed in 2010 and 84 percent of those diagnosed with diabetes are actively managing the disease which requires frequent blood glucose testing. The self-monitoring blood glucose market exceeds $10+ billion per year and continues to grow as does the lifestyle and fitness market which also has great potential.

One of the most significant challenges is that most people with Type 2 diabetes test at least once per day. Diabetics who use insulin (all Type 1 diabetes and many Type 2s) usually test their blood sugar more often (3 to 10 times per day). Testing methods available today require consumers to prick their finger to get a blood sample and then test it. This is painful, inconvenient, and expensive since test strips cost ~ $1 each.



Our product, Socrates Companion™, is the result of scientific research and has patents pending. This device provides a convenient, accurate and pain-free glucose reading that does not require the collection of blood.

2. We see that you have recently launched a fascinating medical technology device, 'Companion'. What was your motivation or inspiration behind developing this innovative technology?

While I do not suffer from Diabetes, my father does and I have witnessed the personal discomfort associated with pricking his finger five-ten times a day to manage his disease.

In addition, I have many close friends whose children suffer from the disease, and see the pain that these children experience – literally transforming the parents' lives and prompting them to become passionate about finding a pain-free solution for their loved ones to manage their condition.

My passion stems from having the opportunity to improve the lives of those who have come before me and those who will come after me.

3. This is definitely great news for many who are afraid of blood and needles. Could you explain the basic core science background of 'Companion™' to our readers?

Socrates uses a patented, Polarimetric approach to determine glucose levels in the blood. By passing light from one side of the top of the ear to the other, Companion™ is able to painlessly measure glucose levels as often as desired by the user – no needles and no blood is required.

Socrates CompanionTM is a patented, small, inexpensive, non-invasive self-monitoring blood glucose monitor device. The device is very simple to operate with a single button and an easy to ready display connected to an ear sensor.

From a financial perspective, diabetics who routinely test their blood spend $30-80 a month on test strips. Companion™'s total cost of ownership will be a fraction of what is being spent today due to its highly efficient design and low recurring associated costs. We are working with insurers to make this device a reimbursable health-care expense.

4. As an entrepreneur, what would you say are the top three priority assets or skill sets needed to be success in the global healthcare industry?

We understand the critical importance of identifying ways to greatly reduce costs in the entire healthcare system. This transcends the continuum of care, from patients to providers to payers – and all of the expenditures for administering efficient care and treatment.

At each step along the way, the goal is to improve the care that providers deliver to their patients, and empower individuals to participate in their own care management and improvement.

High quality products and services must be coupled with effective care coordination and individual care management to ultimately reduce costs for healthcare payers – spanning employers, health plans, government and others. Concurrently, these initiatives will drive better outcomes for consumers of healthcare services.

5. Healthcare industry is one of the most unique fields where collaboration of service providers, researchers, and technology providers is essential. How are you dealing with managing your business networks successfully?

We endeavor to maintain an open dialogue with all stakeholders and are focused on adding value across these networks. For example, we aim to provide the deepest and fastest access to real time data which will support providers' decision making at a level which has never been at their disposal. In the same context, the real time data that is generated from Companion™ will assist researchers in their goal to cure diabetes.

Socrates realizes the complexities of the healthcare delivery system in the US and how it differs dramatically from those throughout the world. In order to address the issues of multiple healthcare industry stakeholders, the Company has assembled a blue ribbon board of directors who have broad reach across the entire continuum of care. Including:

Governor Tommy Thompson
Michael Gorton, healthcare entrepreneur
Patrick Kinder, healthcare delivery executive
Hubert Zajicek, medical technology entrepreneur

6. Our readers are health industry leaders as well as physicians with Korean heritage. Do you have any experience and/or plans of collaborating with Korea or Korean industry?

Absolutely. We are currently in dialogues with three Korean multinational businesses regarding the transformation that Companion™ and the associated technology will have on consumer-based health care.

We have engaged a well-seasoned Korean healthcare consultant who has been instrumental in guiding the Company in capitalizing on business opportunities that may exist within the Korean healthcare business community.

Scott J. Smith
Chief Executive Officer, Founder,
Chairman of the Board of Directors

SOCRATES
HEALTH SOLUTIONS

Scott is the founder,CEO and Chairman of the Board of Directors of Socrates Health Solutions. Scott brings over 20 years of healthcare technology experience to his role at Socrates, with sales and marketing leadership roles with start-up, early emerging and Fortune 100 companies. Prior to launching Socrates, Scott led Global Sales and Marketing for MDG Medical, a medication management device and software company. Scott held sales leadership roles at Curaspan Health Group, United Healthcare, McKesson and Per Se' Technologies with consistent attainment of revenue and operational goals. At VISICU, a leading intensive care software firm, Scott was part of the team that completed a successful Initial Public Offering and eventual sale of the firm. Scott earned his Bachelor of Science degree in Business at the University of Louisiana, Lafayette. In his spare time, Scott enjoys spending time with his three children and long distance running.

City of Hope National Medical Center

Hope starts with a mission: to transform scientific research into new drugs and treatments that will improve as many lives as possible – as soon as possible. At City of Hope, internationally recognized cancer physicians and scientists work together to make an unparalleled difference in cancer treatment. The result is innovative therapies and groundbreaking clinical trials now used by cancer treatment facilities worldwide. It's no surprise that USNews & World Report consistently names City of Hope as one of the best cancer hospitals in the country.

A NEW MODEL OF CANCER CARE

City of Hope is a new model of cancer center, focused on rapidly transforming scientific discoveries into better treatments and better prevention strategies for cancer, as well as diabetes, HIV and other life-threatening diseases. The institution accomplishes this by providing outstanding patient care, conducting innovative research and offering vital education programs focused on eliminating these diseases.

Founded over 100 years ago, City of Hope is one of only 41 comprehensive cancer centers in the nation, the highest designation possible from the National Cancer Institute (NCI). It's also a founding member of the National Comprehensive Cancer Network (NCCN), helping establish research and treatment protocols that affect care nationwide.

The institution's role as a leader in patient care, basic and clinical research, and the translation of science into tangible benefit is supported by a community of faculty and staff committed to changing the future. That community includes scientists, doctors, nurses, health professionals, research associates, graduate students, fundraising specialists, marketing professionals, volunteers and an extensive support staff. All are united by the desire to find cures, save lives and transform health – and by the knowledge that every discovery and every new treatment gives people the chance to live longer, better and more fully.

PROVIDING THE BEST CARE

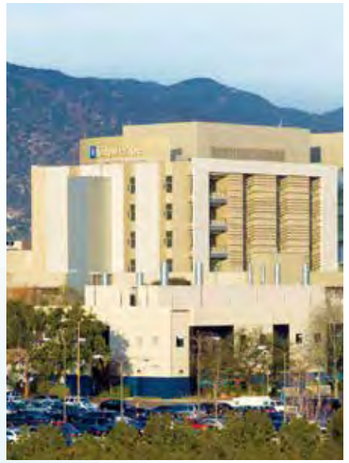
At City of Hope, patients and their families are the priority. When patients are treated right the first time, complications and needless interventions are avoided, outcomes are better, and value is greater. The right diagnosis and treatment plan, along with smooth coordination of care, improves survival and leads to higher patient satisfaction.

Inpatient satisfaction at City of Hope is ranked in the top percentile nationwide. In November 2013, City of Hope received its fourth consecutive Guardian of Excellence Award. This award is given annually to institutions that reach the 95th percentile in patient satisfaction; City of Hope was one of only 26 institutions in the nation recognized. The institution also received the Beacon of Excellence Award, granted to institutions that have maintained consistently high levels of excellence in patient satisfaction for three years.

City of Hope continues to be a pioneer of patient-centered care and remains committed to exceptional care for patients, families and communities.

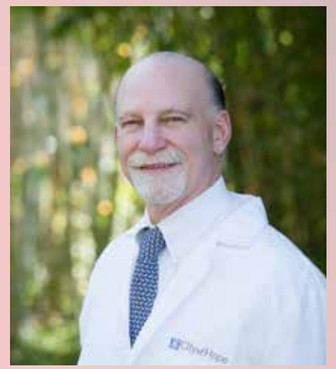
LEADING THE NATION IN PATIENT SURVIVAL RATES

City of Hope's superior patient survival rates were cited as one of the factors in its most recent USNews & World Report ranking. Those rates come from a national database of cancer outcomes that is maintained jointly by the American Cancer Society and the American College of Surgeons' Commission on Cancer. Known as the National Cancer Database, the database allows hospitals to compare their results with results from other hospitals across the nation.



At City of Hope, patient survival rates for many stages of cancer are higher than those at other cancer programs reporting to the Commission on Cancer. These include stages of breast, prostate, urologic, and colon cancers.

Further, City of Hope is a pioneer in the field of hematopoietic cell transplantation (HCT). Its world-renowned team of experts has extensive experience performing a wide variety of transplant procedures—having performed more than 12,000 transplants to date. It is one of the world's largest and most successful stem cell transplant



Steven T. Rosen, MD
Provost and Chief Scientific Officer, City of Hope

ACCELERATING THE PACE OF DISCOVERY

First Provost and Chief Scientific Officer Sets Scientific Direction Steven T. Rosen, M.D., joined City of Hope this past spring from Northwestern University, where he served for 24 years as director of the Robert H. Lurie Comprehensive Cancer Center. Under his leadership, Northwestern's cancer center advanced rapidly, building nationally recognized programs in laboratory sciences, clinical investigations, translational research and cancer prevention and control.

As City of Hope embarks on a new era of strategic growth, Dr. Rosen talks about the efforts he leads to help shape the research and educational vision of the institution.

The Provost/Chief Scientific Officer position is new to City of Hope. How would you describe your role?

In my role at City of Hope, I oversee the Comprehensive Cancer Center, Beckman Research Institute of City of Hope and the Irell & Manella Graduate School of Biological Sciences. I work closely and collaboratively with the scientists, clinicians and administrative leaders to help drive City of Hope's mission.

From my vantage point, I have a broad perspective of all the scientific, medical and educational aspects of City of Hope and am able to coordinate the efforts. Our ultimate goal is always discovery and excellence. I'm charged with ensuring there's continuity as we translate basic science into treatments

centers, improving long-term outcomes for patients diagnosed with leukemia, lymphoma, myeloma and other hematologic malignancies.

As required by the Center for International Blood and Marrow Transplant Research (CIBMTR), City of Hope provides allogeneic transplant data on an ongoing basis. In 2013, the CIBMTR once again reported City of Hope to be an over-performing transplant center in one-year patient survival, a common marker of superior care, the only transplant center in the United States to garner such a distinction for nine consecutive years.

Recently, City of Hope conducted a study (pending publication) that suggested that patients with newly diagnosed adult-onset cancers (cancer occurring between the age of 22 and 65) have superior survival rates when treated at NCI-designated Comprehensive Cancer Centers, such as City of Hope.

As pioneers in the field of robotic surgery, City of Hope's surgeons have performed more than 7,000 robotic procedures for prostate cancer. Its patients have lower lengths of stay and blood loss, with faster recoveries and quicker returns to work.

The robotic expertise doesn't stop there. City of Hope's doctors are now the most experienced in robotic cystectomy, used to treat bladder cancer. City of Hope has even implemented measures to reduce industry-wide variation and establish a new standard in such procedures. Its multidisciplinary care-coordination model provides high-quality, cost effective care to very complex cases. This standard is designed to reduce readmissions, provide team-based care and establish supportive care early in the treatment process.

GROUNDBREAKING RESEARCH

Over the decades, research conducted at City of Hope has led to significant advances in modern medicine, including the development of synthetic human insulin, human growth hormone and the technology behind the widely used cancer-fighting drugs Herceptin, Rituxan and Avastin.

As an independent biomedical, treatment and education center, City of Hope has the infrastructure and collaborative energy to swiftly move from bold, innovative concept to powerful new treatments. Other research distinctions:

- City of Hope is a national leader in translational research, with ideas continuously flowing between investigators and clinicians.
- It has not one, but three on-site manufacturing facilities that enable investigators to manufacture promising new therapies without the high cost and delays encountered by other research centers.
- City of Hope holds more than 200 patents, with more than 30 investigational new drug applications at any given time. These numbers are exceptionally large for an organization of City of Hope's size, reflecting its commitment to innovation and speeding treatments to patients.

Discoveries happen at City of Hope because it fosters an environment that supports intellectual creativity and freedom – the kind of thinking that enables the institution to redefine the future of medical research and medicine.

KOREAN MEDICAL PROGRAM

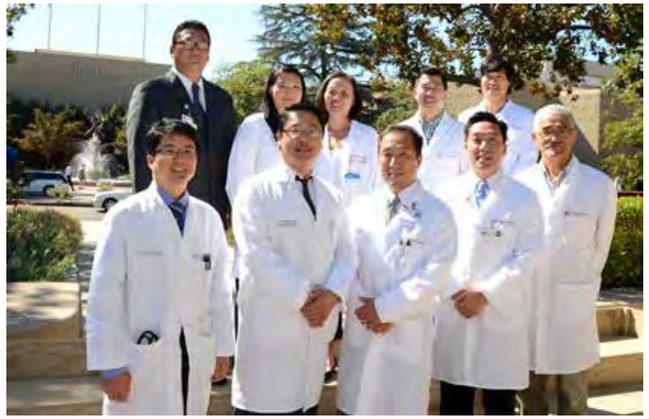
Even though the Korean-American population is increasing in Southern California, few medical centers offer cancer treatment specialties tailored specifically to Korean patients. City of Hope is different.

It is dedicated to providing resources and services to the Korean-American community without cultural and language barriers. Currently, 16 Korean physicians are on staff at City of Hope, providing the best possible cancer services. They are: pathologists Young Kim, M.D., and Joo Song, M.D.; respiratory/critical care physician Anna Kim, M.D.; surgical oncologists Joseph Kim, M.D., Ernest Han, M.D., John Yim, M.D., Jae Kim, M.D., and Robert Kang, M.D.; oncologic radiologists Ji Kim, M.D., and Jinha Park, M.D.; interventional radiologists; John Park, M.D. and Aram Lee, M.D., medical oncologist Christina Yeon, M.D.; anesthesiologist Kenneth Son, M.D.; general surgeon and dermatologist Jae Jung, M.D.; and radiation oncologist Daniel Kim, M.D.

City of Hope also employs many Korean-American pharmacists and nurses.

To further expand the comprehensive treatment services available to Korean-American patients, City of Hope recently entered into a collaborating partnership with Seoul National University Hospital Cancer Center (SNUH). Special programs and services currently in development include a Korean language-based website and recruitment of special translators. SNUH and City of Hope physicians will regularly partner together to optimize the best treatment options by stage of disease in treating Korean patients.

Both Seoul National University Hospital and City of Hope understand that intensive communication increases psychological stability and that emotional and cultural empathy provides clinical benefits.



Korean physicians working at City of Hope. From top left corner to clockwise, Kenneth Son, Jae Jung, Anna Kim, Joo Song, Robert Kang, Young Kim, Jinha Park, John Park, Joseph Kim, Ernest Han.

CONQUERING BLOOD CANCERS

As a world leader in the treatment of blood cancers, City of Hope is now launching an institute specifically focused on researching and treating lymphoma, leukemia and multiple myeloma, as well as other serious blood and bone marrow diseases. Through this institute, laboratory and physician investigators will expand their work and develop new therapies and possible cures for people with leukemia, lymphoma, multiple myeloma and other diseases

The Hematologic Malignancies and Stem Cell Transplantation Institute at City of Hope is built upon a foundation that was created by City of Hope's Stephen J. Forman, M.D., the Francis and Kathleen McNamara Distinguished Chair in Hematology and Hematopoietic Cell Transplantation at City of Hope, and the leader of the institution's Hematologic Malignancies Program, and Steven T. Rosen, M.D., the Provost and Chief Scientific Officer at City of Hope. And next spring, renowned lymphoma and multiple myeloma pioneer, Larry W. Kwak,

What do you see as your priorities in your role?
Our priority has always been to foster investigations that lead to advancements that benefit humanity. Every drug — every treatment — we use today started with an experiment. There is a great history and a strong foundation for discovery here and I am excited to build on it. My priorities are to advance research — to impact as many people as we can and to change the face of the diseases we are working on for future generations.

You have advised many cancer centers. What sets City of Hope apart?
Many institutions have talented investigators, but there are fewer layers here. We can be more creative and respond more quickly to opportunities. We have more resources to advance the mission. People here have a passion about being part of the solution — about being part of the cure, regardless of their role. There's a real culture of optimism and an innate desire to make an impact. I've seen it in individuals before, but not across an entire organization at every level

There is a great deal of science underway at City of Hope. What excites you most?
Not only are we on the leading edge of investigation and discovery here, but we have the core facilities and the talent and commitment to bring those advances forward. There is incredible work underway at City of Hope that can have a revolutionary effect on the way we treat patients and will have an impact on their survivorship. Every day we get a little closer — that's exciting to me.

What attracted you to City of Hope?
I was attracted to the historic strength of the institution — the many discoveries that have stemmed from this place. I was also inspired by the talent that is here and the commitment that there is to be at the forefront and lead the field. City of Hope may be small in comparison to other institutions, but it has the ability to make a national and global impact. We've done it before and it's just a matter of time before we do it again.

M.D., Ph.D., will join City of Hope from MD Anderson Cancer Center. In 2010, Dr. Kwak was selected for his lymphoma vaccine innovation as among Time Magazine's annual list of the top100 most influential people in the world.

Drs. Forman, Rosen and Kwak are known worldwide for the vision, discipline and compassion with which they approach some of the most complex and difficult diseases that afflict men, women and children. All are committed to continuing to make scientific breakthroughs while caring for patients in the uniquely patient-centered environment for which City of Hope is known.

The institute will be composed of six cornerstone centers. Three will be committed to conducting research that will lead to improved treatments for, respectively, lymphoma, multiple myeloma and leukemia. A fourth will be focused on T cell immunotherapy, with its potential to harness the power of the immune system to treat cancer. A fifth is on stem cell transplantation, building on the international reputation of City of Hope as one of the leading transplant programs in the world for curing people who have cancers of the blood and immune system. A sixth will be dedicated to gene therapy. Two of the centers have already been named: The Toni Stephenson Lymphoma Center, named by Emmet and Toni Stephenson and their daughter, Tessa Stephenson Brand; and the Gehr Family Center for Leukemia Research, named by the Gehr Family Foundation, including Norbert Gehr, and his children, Crystal Gehr, Robert Gehr, Max Gehr and Andrew Gehr.

The institute is currently launching several T cell immunotherapy clinical trials for treatment of leukemia and lymphoma, with others being developed for multiple myeloma and novel transplant studies to improve the cure rate for people who need this therapy.

THE NEXT 100 YEARS OF CARE

As City of Hope looks toward its next 100 years, it is more committed than ever to transform the future of medicine. Its researchers, physicians, nurses, educators and staff have made hope a reality for countless patients and their loved ones.

And their work is just beginning.

To learn more about City of Hope, its services and renowned team of experts, visit www.cityofhope.org.

Special Report

SPECIAL REPORT I

GETTING BACK TO THE SCIENTIFIC PRINCIPLES IN CLINICAL DECISION MAKINGS

SPECIAL REPORT II

EYES ON SOUTH KOREA: A RISING PLAYER IN THE GLOBAL BIOPHARMACEUTICAL INDUSTRY

SPECIAL REPORT III

WHY "NEW STANDARD" READY-TO-USE UK INJECTION KIT

Special Report I

Getting back to the scientific principles in clinical decision makings

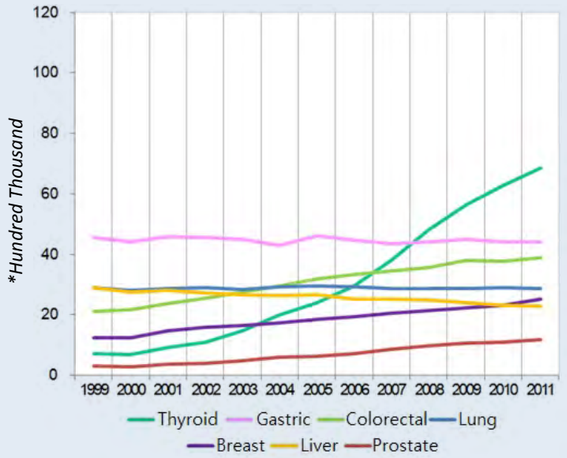
Surge of thyroid cancer

Like many other cancers, thyroid cancer incidence tends to be higher in wealthier regions of the world. The most recent results from International Agency for Research on Cancer (IARC), a cancer-specialized arm of World Health Organization (WHO), confirms that thyroid cancer incidence is higher in North America, Europe, Australia, Japan, and Korea compared to other parts of the world, even with the adjustment of age difference in the populations (1).

2011 Cancer Registry Statistics

2011 Cancer Registry Statistics

Leading cancer type in Age Standardization Incident Rate for Male and Female, 1999 - 2011



Cancer Type	Year		Yearly Change (%)
	1999	2011	
Thyroid	7.2	68.7	23.7*
Gastric	45.5	44.1	-0.2
Colorectal	21.2	39.0	5.6*
Lung	28.9	28.7	0.1
Breast	12.5	25.2	5.9*
Liver	28.9	22.8	-1.8*
Prostate	3.2	11.8	13.5*

** P<.05*

Figure 1. Trend of age-adjusted cancer incidence rate. Modified from a report by Korea Central Cancer Registry, Ministry of Health Welfare, and National Cancer Center

Further, incidence of thyroid cancer has been increasing in many parts of the world. Surveillance, Epidemiology, and End Results Program (SEER), a cancer statistics program in National Cancer Institute, reported that age-adjusted incidence rate of thyroid cancer rose to 14.2 per 100,000 people in 2011 from 7.5 per 100,000 people in 2000 (2). SEER estimates that 566,708 people are living with thyroid cancer in the United States as of 2011. SEER also estimates that 62,980 new cases of thyroid cancer will be diagnosed in 2014. Thyroid cancer is now 10th most common cancer in the United Cancer.

The high rate and the shear increase of thyroid cancer incidence in U.S., however, are no matches for the incidence and the increase thereof in Korea. IARC reported that the age-adjusted incidence rate of thyroid cancer in Korea is 6.4 per 100,000 men and 37.4 per 100,000 women based on cancer cases diagnosed in 2003–2007 (3). The most recent figures from Korean cohort are far worse than these figures. Age-standardized incidence rate of thyroid cancer in Korea, standardized against Korea's population of year 2000, is 24.0 per 100,000 men, 113.8 per 100,000 women, and 68.7 per 100,000 people in year 2011 (4). The average annual increase rate of thyroid cancer incidence is 23.7% during the period from 1999 to 2011 - whopping 9.5 times increase over the 12 year period.

Why is thyroid cancer on the rise?

Facing this unprecedented and unusual increase of thyroid cancer incidence, many clinicians and epidemiologists have tried to answer the question of why thyroid cancer is on the rise. Risk factors like medical X-ray use, diet, life styles, obesity and environmental pollutants have been studied (Table 1). None of the suggested risk factors, however, could explain the surge of thyroid cancer.

Imaging test such as chest X-ray, dental X-ray, and CT scans
Radiation on head or neck to treat cancers
Radioactive materials by nuclear weapon test or nuclear power plant
Pesticides or Persistent organic pollutants (POPs) including polychlorinated biphenyls (PCBs), hexachlorobenzene (HCB), dioxins, and polybrominated diphenyl ethers (PBDEs)
Low consumption of fish, fruits, or vegetables
High consumption of meat, dairy food, or alcohol

Table 1. Suggested risk factors of thyroid cancer

The single most plausible explanation so far is over-diagnosis. Based on a survey on general adult population, Han et al. (2011) reported that 13.2% (8.4% men and 16.4% women) of Korean adults underwent thyroid ultrasonography (5). The authors reasoned that the relative easiness of thyroid sonography both by patient and physician's perspective would play a role in this surprisingly high rate of thyroid sonography in Korea. Thyroid sonography does not require difficult preparations such as fasting and it is relatively easy to perform. Ahn and Park (2009) reported that doctors find thyroid nodules among 22 to 41% of general population using sonography. They also reported that 12% to 22% of people underwent thyroid sonography ended up with the diagnosis of thyroid cancer. With this higher rate of thyroid ultrasonography and surprisingly high rate of discovering thyroid cancer it seems that it is indeed inevitable but ends up with the astronomical incidence of thyroid cancer.

To elucidate the drivers of thyroid cancer screening, Lee et al. (2012) compared the data from 34 wealthier nations (7). They suggested that difference of healthcare system is a factor behind the higher incidence of thyroid cancer. The authors pointed out that a low share of public health expenditure and heavy dependence on patients' direct payment is associated with a high incidence of thyroid cancer. A recent paper noted that the surge of thyroid cancer in Korea began with the screening program initiated and promoted by the Korean government since 1999 (8). The authors also reported a good correlation between percentage of adults reporting being screened for thyroid cancer and incidence of thyroid cancer in Korea.

What are the current recommendations?

In 1996, lacking any controlled study demonstrating that asymptomatic persons detected by screening have a better outcome than those who present with clinical symptoms or signs, the U.S. Preventive Services Task Forces concluded that screening asymptomatic adults or children for thyroid cancer using either neck palpation or ultrasonography is not recommended (9).

Over-diagnosis can cause problems not just through increase of healthcare burdens but also through potential complications associated with the treatment modalities. Potential complication of thyroid surgery includes hematoma, infection, permanent recurrent laryngeal nerve palsy, and permanent hypocalcemia. Further, some patients have to be on lifelong thyroid-replacement therapy following thyroid surgery. Although severe complications are infrequent, one can easily imagine that the actual number of complication is not low given large number of thyroid procedures and burden on patients are severe.

Concerning over potential harm of over-diagnosis Korean experts weighed it against potential gain of thyroid screening. Due to lack of quality evidences showing the harms, however, Korea's experts published relatively moderate and somewhat vague conclusion, "Thyroid cancer screening using ultrasonography in asymptomatic adults is generally not recommended due to insufficient medical and scientific evidences for or against the screening." (10)

Remaining controversies

Despite no recommendation of thyroid cancer screening by both U.S. and Korean experts, there is no sign of changes in clinical practice. Some clinicians advocated the current zealous screening practice and subsequent surgical strategies (11). Some clinicians dismissed the guidelines as unfounded and wrote that patient care should only be based on patient safety not on effectiveness researches (12). Other author recommended downsizing the treatment and suggested use of intervention radiology to manage thyroid cancer instead of opposing routing thyroid cancer screening on a proposition that over-diagnosis is currently unavoidable (13).

The authors arguing for status quo of zealous thyroid screening practices confused on various factors (Table 2).

Lead time bias
Selection bias
Limitation of prognostic measures including survival rate and mortality rate
Multiple comparisons and subsequent finding just by chance
Causal inference based on association

Table 2. Common areas of confusion in the interpretation of cancer data

According to Korean Central Cancer Registry data, 5 year survival rate of thyroid cancer is improved to 99.8% during the period of 2006 to 2010 from 94.9% during the period of 1996 to 2000 (14). Some authors incorrectly attributed this improvement as an effect of early detection and improvement of surgical technique. This improvement in 5 year survival rate is, however, a classic example of lead time bias.

We should note that mortality rate of thyroid cancer in Korea, about 0.5 per 100,000 people, has not been changed over the last decade. A dramatic improvement of survival rate is a consequence of 9.5 times increase in diagnosis of thyroid cancer which has very little impact on mortality rather than a true improvement of survival. In fact, because of the possibility of lead time bias, survival rate is better used in clinical trials where different treatments are compared in similar time period rather than in an evaluation of a cancer prognosis in general without comparison. According to the most recent data of Korean Central Cancer Registry, relative 5 year thyroid cancer survival, a prognosis measure taking into account the effect of deaths from all other causes – is 100.0 percent during the period of 2007 to 2011 (15).

Issue of lead time bias becomes more complicated when combined with other biases or confusions.

Researchers have reported high prevalence of occult prostate cancer – up to 70% for men older than 65, and occult thyroid cancer – up to 36% at autopsy (16 - 18). Because of relative high prevalence in the general population, the likelihood of being identified as a case increases proportionally with the effort to identify the cancer.

Getting back to science

In addition to clinical implications, issues of over-diagnosis can arise in other settings such as lawsuits claiming adverse health effect of alleged exposure to chemicals, radiations, heavy metals, and dusts. The studies performed to identify the factors associated with the cancers are often afflicted with multiple comparisons without proper adjustment. Statistical significance does not necessarily mean that the effect is real. By chance alone about one in 20 attempts will yield a positive finding in popular 95% confidence interval statistical tests.

It seems that some clinicians are frustrated with the new thyroid screening guidelines. But they have to understand that comparative effectiveness research and the guidelines based on careful examination of those studies are one way to ensure a better patient care. Cancer screening is worth only if it detects life threatening cancers among asymptomatic people at a stage when lesions are treatable, and if the benefit from treatment outweighs the potential of harm. As both U.S and Korean experts noted, reliable evidences of benefit from zealous thyroid screening do not exist. The ongoing epidemics of thyroid cancer in both U.S. and Korea are likely an epidemic of diagnosis rather than an epidemic of disease (8, 19). In contentious areas, clinicians and other stakeholders in health should stand firmly on sound scientific principles guarding against common misconceptions.

References

1. International Agency for Research on Cancer. GLOBOCAN 2012: Estimated Cancer Incidence, Mortality and Prevalence Worldwide in 2012.
2. SEER Stat Fact Sheets: Thyroid Cancer. Available at: http://seer.cancer.gov/statfacts/html/thyro.html
3. Age-standardized incidence and cumulative incidence rates and standard errors. Available at: http://ci5.iarc.fr/CI5I-X/old/vol10/CI5-X-All-bySite.pdf
4. National Cancer Information Center of Korea. Cancer Incidence Trend Analysis. Available at: http://www.cancer.go.kr/mbs/cancer/subview.jsp?id=cancer_040104000000
5. Han MA et al. Current Status of Thyroid Cancer Screening in Korea: Results
From a Nationwide Interview Survey. Asian Pacific J Cancer Prev. 2011;12:1657-1663
6. Ahn HW and Park YJ. Incidence and clinical characteristics of thyroid cancer in Korea. The Korean Journal of Medicine. 2009;77(5):537-542
7. Lee TJ et al. The Incidence of Thyroid Cancer Is Affected by the Characteristics of a Healthcare System. J Korean Med Sci. 2012; 27: 1491-1498
8. Ahn HY et al. N Engl J Eed. 2014;371(19):1765-1767
9. The U.S. Preventive Services Task Force. Guide to Clinical Preventive Services: Report of the U.S. Preventive Services Task Force. 2nd Edition.
10. Committee on Revision of Thyroid Cancer Screening Guideline. Thyroid Cancer Screening Guideline (Draft). August 2014.
11. Doctor's News. Thyroid Cancer Guideline, Wrong From the First Button. Available at: http://www.doctorsnews.co.kr/news/articleView.html?idxno=98646
12. Chung JH 2014. A Refutation against Unfounded Reports on Thyroid Cancer. J Korean Thyroid Assoc. 2014;7(1):1-6
13. Mauri G 2013. In response to Thyroid cancer: zealous imaging has increased detection and treatment of low risk tumours. BMJ 2013; 347. Available at: http://www.bmj.com/content/347/bmj.f4706/rr/663585
14. National Cancer Information Center. Treatment situation. Available at: http://www.cancer.go.kr/mbs/cancer/jsp/cancer/cancer.jsp?cancerSeq=3341&menuSeq=3360&viewType=all&id=cancer_020112000000
15. Korean Central Cancer Registry. National Cancer Registry Statistics 2011.
16. Haas GP et al. The Worldwide Epidemiology of Prostate Cancer: Perspectives from Autopsy Studies. Can J Urol. 2008;15(1):3866–3871
17. Harach HR et al. Occult papillary carcinoma of the thyroid: a "normal" finding in Finland — a systematic autopsy study. Cancer 1985;56:531-8
18. Yamamoto Y et al. Occult papillary carcinoma of the thyroid: a study of 408 autopsy cases. Cancer 1990;65:1173-9
19, Davies L and Welch HG. Current Thyroid Cancer Trends in the United States. JAMA Otolaryngol Head Neck Surg. 2014;140(4):317-322

Doug Yoon, MD, PhD, MBA
Founder, Washington Scientific

Dr. Yoon is the Founder and Chief Scientist of Washington Scientific. Washington Scientific specializes in application of scientific principles and risk management strategies to medical, environmental health, and pharmaceutical areas. Dr. Yoon provides critical scientific insights to clients, often in a multinational and multicultural setting, by utilizing his medical and epidemiological expertise. Dr. Yoon's work includes evaluation of epidemiological studies involving cancer or other chronic diseases; developing strategies to estimate health outcomes using health insurance claim data; evaluation of specificity and alternative causes of medical conditions; analyzing environmental exposure modelings; evaluation of admissibility of scientific evidences in courts based on human, animal and in vitro evidences; examination of causation criteria and disease susceptibility claims; and evaluation of medical treatments or guidelines through the principles of evidence based medicine.

Dr. Yoon is a strong advocate for humanitarian actions. He has participated and led medical relief actions responding various disasters including the 2005 tsunami and the 2006 earthquake. As of November 2014, Dr. Yoon is selected as a member of the Korean government's effort to fight against the Ebola outbreak in West Africa.

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Special Report II

Eyes on South Korea: A Rising Player in the Global Biopharmaceutical Industry

South Korea was highlighted as a collaboration destination at the Trans-Pacific Health Sciences Dialogue held in Philadelphia from September 16 and 17. This specific health science dialogue is a C-level meeting for biopharmaceutical industry executives who want to accelerate, explore and develop collaborations and partnerships with their counterparts in the most important Trans-Pacific health care markets including Japan, China, Korea and North America. Over the course of two days, executives, investors, and experts shared their insights and experiences to discuss current trends, issues with panel discussions and case studies that targets growth, achieves objectives, adds value and minimizes risk on both sides of the Pacific.

A session titled South Korea: A Rising Player in the Global Biopharmaceutical Industry focused on exploring collaboration opportunities of Korea. This session was moderated by Dr. Do Hyun Cho, CEO and President W Medical Strategy Group, and discussed by two other panelists Mr. Han Bang, managing director from Betachem Inc., and Dr. Tae Wan Kim, Professor at the Columbia University Medical School.

competitiveness of Korean drug industry in global market

Dr. Cho discussed about the status of Korea BioPharmaceutical industry and its competitiveness in the global market. Current governmental policies were introduced and the vision of Korea BioPharmaceutical industry was discussed. Mr. Bang explained the competitiveness of Korean drug industry in global market and introduced examples of factors that make Korea such competitive and attractive collaboration partner. Dr. Kim discussed about the factors why experts favor Korea as a hub for global R&D collaborations and why other alliances such as infrastructures & financials are well-developed in South Korea. He compared Korean industry to other developed industry and explained about the productivity in R&D and how to overcome the cultural barriers in deal process.

This session provided many potentials of Korea as prospective partner with global companies through Public Private Partnership, R & D investment, and clinical trials. Many audiences who attended the session showed their interest towards collaboration with Korea. W

Special Report III

WHY "NEW STANDARD" Ready-to-use *UK Injection Kit*

UK Do-i, a Korea based pharmaceutical holding company is currently in process of establishing a local manufacturing facility through its U.S. subsidiary BNCP Corporation. UK Chemipharm, another subsidiary pharmaceutical company based in Korea, had been developing Ready-to-Use UK Injection Kit (Full Kit) and Half Injection Kit (Half Kit). UK Chemipharm is the current manufacturer and distributor of their product within Korea and overseas. After establishment of its first U.S. office 10 years ago, UK Do-i came along a long and challenging journey to become the first Korean Pharmaceutical company to build an Injectable cGMP manufacturing facility in the U.S. UK Do-i believes that their kit will be the new global standard product in injectable industry.

UK Do-i Co.,Ltd.

UK Chemipharm Co.,Ltd.

BNCP Corporation

With major investments from UK Do-i, and funding(equity finance) through BNCP Corporation, Indiana State's bond finance and County incentive programs, UK Do-i have bought 52,400sqft building site and 12 acres of land for their pharmaceutical facilities. With budget of 30 million dollars, construction will be started in March 2015 and completed by end of that year.

It is expected to receive U.S. FDA's full approval on facility and product within 2017. Distribution and sales of products in the U.S. and Canada are expected to start in 2018, and target regions will be expanded into EU and Latin American countries.

Within three years after product approval of U.S. FDA, sales are expected to grow over 30 million units of UK Injection Kits which will generate $180 million dollars in revenue. And within five years, it is expected to grow to reach 50 million units of UK Injection Kit and $300 million dollars in revenue. UK Do-i is aiming to reach 10 % of market share in the antibiotic injection industry after 5 years of sales activities.

UK Injection Kit has its unique strength which serves unmet need of existing device and process. Normally there are around seven burdensome steps in preparing and administering an injectable product; 1) preparation of medicine and dissolution equipment 2) unsealing medicine and dissolution equipment 3) dissolve under disinfection environment 4) labeling 5) priming 6) administer injection 7) disposal. These seven steps are widely exposed to variety of difficulties and problems including but not limited to; possibilities of contamination due to microbial, unintended mix of foreign substances, human error and other burdens including high demand on time and budget input. To decrease the risk and time, many drug manufacturers have developed numerous ready-to-use products and UK Injection kit is one of the most advanced and innovative form of ready-to-use products in the current market.

UK Chemipharm has been researching and developing since 2000 to make the most efficient IV injection kit. After four years of development, UK Chemipharm has successfully came up with its final edition of the kit with its patents in Korea, U.S., Canada,, EU, China, and Mexico, and Patent Pending under review in India, Brazil and UAE, etc. The core technology and a huge benefit of this product is that any existing vial is attachable to the ready-to-use kit. This allows much more flexibility to expand the products portfolio because the vial component of UK Injection Kit can be utilized by any standard size vial that is being sold on market.
Another core technology is the connection part of between vial and solution as Saline, Dextrose and WFI, etc. It is an aseptic connection set which prevents any germs to infiltrate while mixing vial to the solution. Plastic needle on the connection part is bidirectional. Just one-touch pushing the needle from solution bag side, rubber stopper is penetrated and both side connected with bidirectional needle. With pumping the solution bag lightly, solution is transferred to the vial and mixed with the powder in vial. Then by the just same way (pumping solution bag lightly), the constituted solution is re-transferred to the solution bag and ready to IV infusion set.

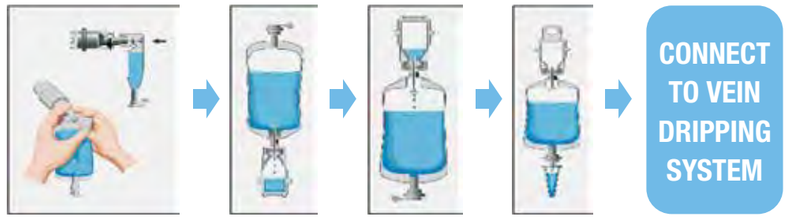
From 2004, UK Chemipharm has obtained marketing authorization for Cefmetazole, Vancomycin, Imipenem/Cilastatin, Cefotiam, Ceftriaxone, Cefoperazone/Sulbactam, Teicoplanin, Ceftizoxime, Cefotetan UK injection kit from KFDA and launched these products in Korea and Japan.
Also, UK Chemipharm is currently working on developing FLOMOXEF Na and MEROPENEM injection kit.

These products are very popular among nurses, doctors, and pharmacist and especially have strengths in same areas where international assessment criteria also emphasizes, including minimizing infection risk, safety from needle injury, and no leakage of any solution which will reduce any allergy occurrence among the users.

UK Chemipharm's most innovative UK Injection Kit allows any users to constitute the vials and solutions in a closed system. Any foreign substances or bacteria that have risk of contaminations are blocked by our product to provide safety and reduce the possibilities of infection. This will reduce any further treatment costs which can be generated by infection complications. It will also reduce needle injury and allow safe preparation to make solutions in short period of time which also reduces costs for inventory management and waste disposal for any unnecessary materials that were previously used for preparation.

Thus, followings can be emphasized as the benefits of this product;

1. Closed system applicable for USP chapter(797)
2. Reduce the risk of microbial contamination
3. Faster preparation time with ready to mix system
4. Reduce the needle injury and antibiotic allergy of practitioner
5. Wide range of antibiotic product portfolio
6. And more innovations & advantages



Below document was published few years ago and it shows infection and other problematic issues with injectable products;

A) Hospital-Acquired Infection is…
An infection caught while hospitalized. Most nosocomial infections are due to bacteria. Since antibiotics are frequently used within hospitals, the types of bacteria and their resistance to antibiotics is different than bacteria outside of the hospital.
A nosocomial infection is strictly and specifically an infection “not present or incubating prior to admittance to the hospital, but generally occurring 72 hours after admittance
U.S. Center for Disease Control and Prevention (CDC)

B) Nosocomial Infection rate of 15 general hospitals in the entire domestic area
- Patients discharged from hospitals: 3.7%
- Entire hospitals: 5.8% ~ 15.5%
- Intensive Care Unit (ICU): 10.5% ~ 39.7%
- Patients who had a surgical operation: 5.6% ~ 9.8%

** Korean Society for Nosocomial Infection Control*

C) Endogenous Infection (67% from total HAI): when patient’s immune ability is declined, it is occurred by bacteria that patient already have in their body
Exogenous Infection (33% from total HAI): can be prevented by infection control
Not possible to prevent 100% of Hospital-Acquired Infection
U.S. Center for Disease Control and Prevention (CDC)

D) In hospital ward-based preparation of IV medicines:
Certain risks by nursing or medical staff: Errors in dose preparation and administration as a result of frequent interruptions, cramped working areas and lack of time. (26.9% of error rate for the preparation of IV drugs)
Incompatibility or instability due to use of incorrect diluents, or inappropriate storage
Potential hazards to nursing staff from needlestick injury
Preparation of a single IV dose has been measured at between 3 to13 mins

E) Needlestick Injury’ - Parenteral introduction of blood or other infectious material into the body, of usually nursing, laboratory staff and physicians during the performance of his or her duties, by a hollow-bore needle, or sharp instrument, including, but not limited to, needles, lancets, scalpels and contaminated glass
12 billion injections are administered each year worldwide
Over 3 million people are injured by accidental needlestick injury
Hepatitis B, Hepatitis C, HIV and AIDS are the main viruses implicated in needlestick injury
****World Health Organization (WHO)***

F) No. of using injections: 12 billion/yr
- U.S. 17%, Japan 13%, EEA 35%
Ratio of using ready to mix system: 10%
- U.S. 25%, Japan 15%, EEA 20%

Because this product was the solution to above problems, UK Chemipharm and its product line has been expanding its business throughout Korea and Japan. UK Chemipharm is currently distributing to over 100 general hospitals in Korea and reached $10 million revenue in 2013. Also in 2013, UK Chemipharm contracted with with Daewoong Pharmaceutical to co-promote this product. This year, it is expected to grow over $ 20 million dollar sales and by the end of next year with new product launched, it is expected to reach $40 million dollars. Current production lines are being operated two shifts a day and 6days a week due to dramatic growth in the market and construction of new manufacturing facilities are scheduled next year.

State of the art
UK Injection Kit

After receiving BGMP and KGMP in 2003, UK Chemipharm maintained stable net profit which led to continuous investment in research and development. They were able to provide various portfolios and launch new products consistently. UK Do-i’s long term goal of entering U.S. is now actualized, and they are in process of strategic partnership with several big antibiotic drug vial manufacturing companies.

Gibum Oh
CEO, UK Do-i Co., Ltd.

Gibum Oh is the CEO of UK Do-i and its subsidiary companies; UK Chemipharm, UK Ucera, Kacel, BNCP USA Corp., BNCP China Corp. UK Chemipharm manufactures and R&D for FDF(Finished Dosage Form) and API(Active Pharmaceutical Ingredient). UK Ucera manufactures and supply thermal protectors for electronics. Kacel manufactures and distributes tungsten carbide tools and develops PVD coating technology. BNCP USA is in charge of marketing for North and South America and Europe. BNCP China is in charge of marketing and R&D in China.

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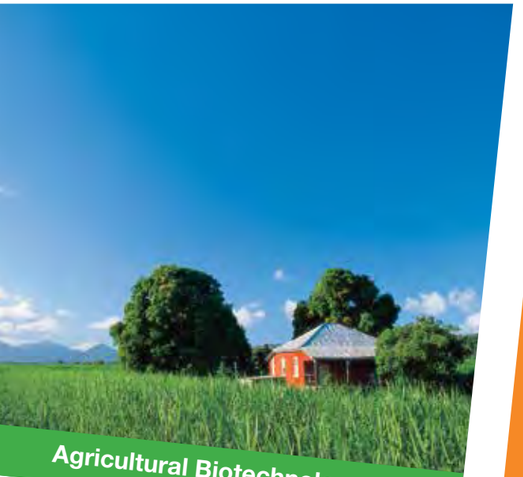

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Bio Pharmaceutical Report I

Array/Novartis' binimetinib expected to best chemotherapy in Phase III trial despite protocol changes

- Enrollment criteria expanded mid-trial to reflect shifting treatment landscape
- Inhibiting MEK elicits enthusiasm for NRAS patients considering lack of options
- Chemo comparator, PFS as primary endpoint will suffice for approvals if results positive

Array BioPharma (NASDAQ:ARRY) and Novartis (VTX:NOVN) can expect MEK inhibitor binimetinib (MEK162) to meet the primary endpoint in a Phase III trial in NRAS Q61-mutant melanoma, experts said. Yet, they noted, binimetinib will not make as big of a difference to this patient population as BRAF inhibitors did for BRAF-positive patients.

Despite protocol amendments to reflect the rapidly changing treatment landscape and include treatment-experienced patients, experts said the trial (NCT01763164) is designed well enough to meet the progression-free survival (PFS) primary endpoint compared to chemotherapy dacarbazine.

Though binimetinib's data so far in NRAS patients does not seem to be as good as efficacy results seen with BRAF inhibitors for the BRAF population, MEK inhibition is a good enough option. NRAS-mutant melanoma patients represent less than 20% of advanced melanoma patients, as the majority harbor BRAF mutations, and this smaller population represents a significant unmet need for targeted therapy, experts agreed.

Much of the optimism for the study showing a PFS benefit is based on the response rate seen in a Phase II trial compared to the known response rates of chemotherapy in the NRAS population, experts said.

While a chemo comparator is not the best for newly diagnosed patients, it is acceptable for previously treated patients and along with PFS used as the primary endpoint, could be sufficient for approval.

The trial was initiated in July 2013, and primary outcome data will be collected December 2014, according ClinicalTrials.gov.

The company declined to comment.

Trial design valid despite protocol amendments

The global Phase III trial dubbed NEMO pits binimetinib against dacarbazine in NRAS patients with a Q61 positive mutation. This mutation can be compared to the V600 mutation among BRAF patients, in that it is the most common mutation among the NRAS group, experts said. The Q61 mutation was tested locally but confirmed with Novartis' in-house diagnostic at a central lab, said investigator Dr Christian Blank, assistant professor, Department of Medical Oncology, Netherlands Cancer Institute.

The trial was initiated in July 2013, and the protocol was amended due to a rapidly changing regulatory landscape, noted Blank. Bristol-Myers Squibb's (NYSE:BMY) immunotherapy Yervoy (ipilimumab), approved in the US in March 2011, is the preferred first-line treatment for many NRAS patients. While the drug was also approved in the EU in 2011 as a second-line treatment, it was expanded into the first-line setting in November 2013. The EU expansion prompted a change in NEMO's protocol to include both treatment-naive and treatment-experienced patients, said Dr Paolo Ascierto, who is on the trial steering committee and is vice-director,Unit of Medical Oncology and Innovative Therapy, National Tumor Institute Fondazione G. Pascale, Naples, Italy.

The protocol was altered to more closely mirror clinical practice, in which binimetinib would likely be used after Yervoy failure, said Blank. Patients were randomized 2:1 to the binimetinib or dacarbazine arms and are stratified according to whether they are immunotherapy-naïve or not.

The trial is thus designed to capture differing response rates between treatment-naïve and treatment-experienced patients, experts added. Previously treated patients will likely see worse outcomes because they are further along in disease progression, said Dr Alexander Spira, oncologist, Virginia Cancer Specialists, director, VCS Research Program. However, Blank said, the response rates might not be significantly different between these two groups.

Experts were positive on the prospect of superior PFS for the treatment arm as a whole compared to the chemo arm. However, secondary endpoints including OS may be influenced by the immunotherapy patients receive after trial completion, said Blank, and Dr David Minor, associate director, melanoma research, California Pacific Melanoma Center, San Francisco.

While OS may be confounded by post-trial treatments, the US-based trial investigator noted there are few options for NRAS patients after immunotherapy or MEK inhibition, and therefore OS will still be a meaningful endpoint.

MEK inhibition for NRAS a good strategy

Based on the results of the Phase II study in 71 patients with either BRAF or NRAS mutations, the concept of using MEK inhibitor as a targeted therapy in NRAS patients is fairly promising, said Dr Ryan Sullivan, oncologist, Massachusetts General Hospital Cancer Center, Boston.

The Phase II trial demonstrated a 20% partial response rate for separate NRAS and BRAF groups at 3.3 months [Lancet Oncol. 2013 Mar ;14(3):249-56. doi: 10.1016/S1470-2045(13)70024-X. Epub 2013 Feb 13]. None of the patients showed complete responses at the time the data was collected.

Despite the similar response rates for the two subgroups, a successful Phase III trial in 393 NRAS-only patients would be the first demonstrated effective targeted therapy for the minority group, experts agreed.

A 20% response rate is going to be fairly consistent moving into the Phase III trial, said Dr Robert Conry, associate professor, medicine, University of Alabama at Birmingham. The MEK inhibitor binimetinib in an NRAS patient does not

Secondary end points in the trial include safety as well as impact on health-related quality of life and use of healthcare resources.

appear to be as much of a home run as a BRAF inhibitor in a BRAF patient but still represents a promising enough level of activity to bode well for Phase III, said Minor. It is hard to predict results with certainty, but the Phase III trial is designed well enough to show similar outcomes of the approximate four-month PFS and 20% response rate that was observed in Phase II, Sullivan said.

If you consider that, historically, PFS is 1.7 months with dacarbazine, and PFS in the Phase II trial reached about 4 months, it is likely binimetinib will yield superior PFS, Ascierto said. Based on Phase II results, of which Ascierto was the lead author, the 45mg twice-daily dose used in Phase III represents the best balance of efficacy and safety, he noted. Toxicity does not appear to be a serious concern, experts noted.

While RAS mutations are present in a number of cancers, they are the most common in melanoma, said Dr Wilson Miller, deputy director, Segal Cancer Center, McGill University, Montreal, Canada. Binimetinib is likely to show benefit for this population as the first targeted single agent, he added.

Chemo comparator, PFS will suffice for approval

When the Phase III trial was originally designed, Yervoy was a second-line treatment in Europe, so to avoid any possible treatment that might confound results after disease progression, PFS was chosen as the primary endpoint, said Ascierto. Normally, overall survival (OS) would be preferred, but PFS will be a clear indicator of efficacy, he continued. Blank agreed PFS will be a good indicator.

The inclusion of treatment-naïve and treatment-experienced patients does not negatively impact the trial's potential to show a significant PFS benefit, experts said.

Even though recruitment might be difficult with a chemotherapy comparator arm, it is still viewed as a valid comparator in terms of regulatory approvals, noted Miller.

Enrollment has not been a problem since the protocol change, Ascierto noted. And now, considering the recent clinical development and US market entry of Merck's (NYSE:MRK) anti-PD1 immunotherapy Keytruda (pembrolizumab), there are an increasing number of patients who have received two prior immunotherapies.

Novartis has a market cap of of CHF 240.1bn (EUR 198.9bn), and Array has a market cap of USD 514.2m. W

Sony Salzman

Reporter, BioPharm Insight

Sony previously worked as the Managing Editor for MedTechBoston.com, a publication covering Boston's medical innovation landscape. She holds a master's degree in Science Journalism from Boston University and has won awards in both narrative writing and radio journalism. Additionally, Sony worked as a reporter for MassDevice.com, a wire service covering the medical device industry, and as a research intern for NOVA, a PBS program produced by Boston's WBUR. She also was a freelance journalist and her stories have been featured by organizations such as the Boston Globe, WBUR (Boston's NPR news station) and TechCrunch.com.

Bio Pharmaceutical Report II

J&J may suffer over AbbVie, Amgen in renewed biologic US payer contracts as Celltrion's biosimilar looms

- Remsima use may be forced ahead of Remicade, but not Humira or Enbrel
- Celltrion needs to emphasize Remsima clinical comparability to innovator
- Low uptake expected in GI indications if Remicade label not fully extrapolated

Johnson & Johnson (NYSE:JNJ) may struggle more than AbbVie (NYSE:ABBV) and Amgen (NYSE:AMGN) in renewed US pricing contracts for biologics as biosimilars enter the market, experts said. All candidates are likely to soon face tougher payer negotiations, particularly with the expected market entry of Celltrion's (KOSDAQ:068270) biosimilar Remsima, they added.

Compared to AbbVie's Humira (adalimumab) and Amgen's Enbrel (etanercept), Johnson & Johnson's (J&J) Remicade (infliximab) could face a greater challenge in retaining market share considering its intravenous route of administration, they said. Still, J&J may have a slight reprieve if the FDA does not allow Remsima full label extrapolation of Remicade, they added.

This news service recently reported an FDA regulatory nod is expected for Remsima, anticipated for August 2015. The product is the first monoclonal antibody (mAb) application to undergo the US biosimilar pathway, and the second drug filed under the pathway, according to a release.

Johnson & Johnson may struggle more than AbbVie and Amgen in renewed US pricing contracts for biologics as biosimilars enter the market...

Pricing and contracting strategies

While Remicade may not be the preferred first-or second-line biologic in rheumatoid arthritis (RA), it generated revenue of nearly USD 4bn in the US last year and was the third-biggest selling drug globally, said Kate Keeping, UK-based senior director of biosimilars research at Decision Resources Group. There is an expectation of minor cross-brand erosion to Humira and Enbrel once there are infliximab biosimilars, but the vast majority of patient share will be captured from Remicade, Keeping and a US reimbursement consultant agreed.

The majority of market share has been shifting between Enbrel and Humira and relative cost is part of that shift, said a second US drug consultant. Whether or not payers decide to replace the branded products with biosimilars will depend upon their view of the safety and efficacy combined with the savings opportunity, he added.

In general though, payers will particularly use biosimilars in the RA class as Remicade, Enbrel and Humira were in the top 10 drug costs in 2013, said Rhonda Greenapple, founder, New Jersey-based reimbursement consultancy Access First.

If Celltrion offers an agreeable price to payers, step therapy that forces Remsima use ahead of Remicade is likely, but is significantly less likely to be applied to other anti-tumour necrosis factors (TNFs) alphas such as Enbrel and Humira, according to payers Decision surveyed this year, Keeping noted. This is because Remicade has additional costs as an office-administered product versus self-injectable Humira and Enbrel, the first consultant and Greenapple agreed.

Remicade is the "big loser" in terms of market share versus the biosimilar, as well as versus Humira and Enbrel, due to its additional office costs, the first consultant said.

All three drug costs vary between patients and individual regimes but can cost in the range of USD 20K-30K per patient/year. But Remicade's additional office cost makes it "much more expensive" than Enbrel and Humira, therefore step-edits that force biosimilar use first are likely, said Dr Nathan Wei, rheumatologist and founder, Arthritis Treatment Center, Frederick, Maryland.

Humira and Enbrel dominate as the preferred biologics (followed by Remicade) due to aggressive contracting that has them as preferred status over other brands, Greenapple added. Contracts are based on market share, drug volume, preferred access and price ceilings, she said.

AbbVie and Amgen could offer a price discount in the neighbourhood of 30% as part of contract renegotiations, depending on the formulary plans' size and level of control, Greenapple said. Besides a price discount, the manufacturer can bundle contracts together so as to offer discounts across a wide variety of product areas, in turn for preferred formulary status, the consultant said. Manufacturers will likely wait to see biosimilars' impact on market share to drop their prices, Greenapple said.

Remsima uptake could be low initially since its competitor products are contracted by commercial insurers for price protection, and

The majority of market share has been shifting between Enbrel and Humira and relative cost is part of that shift

preferred drug formulary status policies have fixed contract term lengths of time associated with them, said Charles Shasky, president of Virginia-based pharmacoeconomics consultancy Biotechnomics.

When these confidential contracts expire, greater biosimilar uptake would be expected, he said. If Celltrion starts negotiations with the insurers today, it may take a year or two to complete negotiations, he said. Innovators could also lobby to influence state-dispensing laws and regulations so as to steer away from biosimilar substitution, Shasky noted.

Celltrion needs to convince physicians and payers that Remsima is clinically comparable to Remicade first and foremost, Keeping and the second consultant said. Both stakeholders cite concerns on efficacy and safety/immunogenicity as the leading barriers to biosimilar use, Keeping noted. Company promotion of data that supports product comparability is "hugely important," for clinical and nonclinical characterization and product quality, Keeping and the second consultant noted.

"Janssen [J&J] remains confident in the position of Remicade and the value of this differentiated anti-TNF-alpha treatment," a spokesperson said, noting the safety and efficacy has been well-established through extensive clinical development programs, postmarketing surveillance, registries and commercial experience. To date, sales of biosimilar infliximab agents have been limited despite the EMA's approval in September 2013, he added.

Amgen declined to comment on commercialization questions.

Off-label considerations

Remicade is indicated in the US for paediatric and adult Crohn's disease (CD), paediatric and adult ulcerative colitis (UC), RA, psoriatic arthritis (PA), ankylosing spondylitis (AS) and plaque psoriasis (PS).

There is debate on whether Celltrion's previous positive data in RA and other indications can be extrapolated to CD and UC, this news service previously reported. Health Canada did not permit full indication extrapolation while the EMA did, the experts noted. Health Canada approved Remsima in April for RA, AS, PA and PS. Celltrion announced on 28 June 2013 that the EMA's Committee for Medicinal Products for Human Use (CHMP) had given positive opinion for Remsima.

Celltrion submitted to the FDA the same evidence it did to the EMA to resolve concern on indication extrapolation, a Celltrion spokesperson said. The firm believes it will get full label extrapolation, including for gastrointestinal (GI) conditions, he added. The firm is running a global clinical trial to assure physicians that Remsima is clinically comparable to Remicade for GI patients, he added. A 214-patient, randomized, double-blind, switching study (NCT02096861) in active CD patients started in July and ends in March 2017, according to ClinicalTrials.gov.

If the molecule is not approved for CD/UC at the time of launch, the expectation is there will be very low uptake in the gastroenterology indications, Keeping said. A gastroenterologist survey conducted by Decision Resources indicates a low likelihood of biosimilar use in an off-label indication and there is a possibility that it wouldn't be reimbursed for off-label indications by all US insurance plans, she said.

Payers would ultimately determine use, and physicians would unlikely use the biosimilar off-label, agreed Dr Stephen Hanauer, professor in Medicine-Gastroenterology and Hepatology, Northwestern University Feinberg School of Medicine, Chicago, Illinois and previous chair of the FDA's Gastrointestinal Drugs Advisory Committee.

Payers generally will not pay for off-label use unless there is a minimum of three independent publications substantiating that the product works in that area, said the first consultant. Shasky noted off-label reimbursement can potentially be seen by the public and the FDA as the insurer superseding the agency's expertise.

Yet payers have approved off-label indications for Teva Pharmaceutical Industries' (NASDAQ:TEVA) Granix (tbo-filgrastim) -- a "copy" of Amgen's neutropenia drug Neupogen (filgrastim) -- despite not being eligible under its 351(a) BLA filing route, Greenapple said. There may, however, be more hesitancy to make a similar decision for a mAb, she added.

Celltrion's market cap is KRW 4.6bn (USD 4.4m). W

Jennifer C. Smith-Parker

Reporter, BioPharm Insight

Jennifer is an award-winning biopharmaceutical industry journalist. Prior to joining BioPharm Insight Jennifer was Associate News Editor at FDA Week, covering FDA regulatory policy for all FDA-regulated product areas. She also worked at The Monitor, where she covered health, environment and science issues and conducted a year-long project on indigent healthcare services. She was awarded the Texas Medical Association's Anson Jones journalism award for an article on breast cancer. Jennifer graduated from New York University with a Bachelor's with Honors in History and Journalism.

Jinan was a freelance journalist before joining BioPharm Insight, writing for numerous magazines and websites covering health and science stories. She has a BSc in Physiology from King's College London and an MA in Science Journalism from City University London.

Not an actual patient, but is representative of a real patient type. Models are used for illustrative purposes only.

IN THE TREATMENT OF CHRONIC HEPATITIS B (CHB) IN ADULTS WITH COMPENSATED LIVER DISEASE

TAKE A CLOSER LOOK AT LAMIVUDINE (LAM) RESISTANCE

MORE THAN 50% of Americans living with CHB are Asian and Pacific Islanders[1]

NEARLY 70% of Asian Americans were born or have parents born in countries where CHB is common[1]

70% of patients receiving lamivudine develop resistance at 5 years[2]

2% of patients in the United States use lamivudine; **up to 88%** in Asia[3]

Indication and Usage

VIREAD® (tenofovir disoproxil fumarate) is indicated for the treatment of chronic hepatitis B in adults and pediatric patients 12 years of age and older.

The following points should be considered when initiating therapy with VIREAD for the treatment of HBV infection:

- The indication in adults is based on data from treatment of subjects who were nucleoside–treatment-naïve and treatment-experienced with documented resistance to lamivudine. Subjects were adults with HBeAg-positive and HBeAg-negative chronic hepatitis B with compensated liver disease
- VIREAD was evaluated in a limited number of subjects with chronic hepatitis B and decompensated liver disease
- The numbers of subjects in clinical trials who had adefovir resistance-associated substitutions at baseline were too small to reach conclusions of efficacy

Important Safety Information

BOXED WARNING: LACTIC ACIDOSIS/SEVERE HEPATOMEGALY WITH STEATOSIS and POST TREATMENT EXACERBATION OF HEPATITIS

- **Lactic acidosis and severe hepatomegaly with steatosis, including fatal cases, have been reported with the use of nucleoside analogs, including VIREAD, in combination with other antiretrovirals**
- **Severe acute exacerbations of hepatitis have been reported in HBV-infected patients who have discontinued anti-hepatitis B therapy, including VIREAD. Hepatic function should be monitored closely with both clinical and laboratory follow-up for at least several months in patients who discontinue anti-hepatitis B therapy, including VIREAD. If appropriate, resumption of anti-hepatitis B therapy may be warranted**

Warnings and Precautions

- **New onset or worsening renal impairment:** Cases of acute renal failure and Fanconi syndrome have been reported with the use of VIREAD. In all patients, assess estimated creatinine clearance (CrCl) prior to initiating and during therapy. In patients at risk for renal dysfunction, including those who previously experienced renal events while receiving adefovir dipivoxil, additionally monitor serum phosphorus, urine glucose, and urine protein. In patients with CrCl <50 mL/min, adjust dosing interval and closely monitor renal function. Avoid concurrent or recent use with a nephrotoxic agent. Cases of acute renal failure, some requiring hospitalization and renal replacement therapy, have been reported after initiation of high dose or multiple NSAIDs in HIV-infected patients with risk factors for renal dysfunction; consider alternatives to NSAIDs in these patients. Persistent or worsening bone pain, pain in extremities, fractures and/or muscular pain or weakness may be manifestations of proximal renal tubulopathy and should prompt an evaluation of renal function
- **Coadministration with other products:**
  - Do not use in combination with other products containing tenofovir disoproxil fumarate
  - Do not administer in combination with adefovir dipivoxil
- **Patients coinfected with HIV-1 and HBV:** Due to the risk of development of HIV-1 resistance, VIREAD should only be used in HIV-1 and HBV coinfected patients as part of an appropriate antiretroviral combination regimen. HIV-1 antibody testing should be offered to all HBV-infected patients before initiating therapy with VIREAD
- **Bone effects:** Decreases in bone mineral density (BMD) and mineralization defects, including osteomalacia, have been seen in patients treated with VIREAD. Consider assessment of BMD in adult and pediatric patients who have a history of pathologic bone fracture or other risk factors for bone loss. In a clinical trial conducted in pediatric subjects 12 to <18 years of age with chronic hepatitis B, total body BMD gain was less in VIREAD-treated subjects as compared to the control group. In patients at risk of renal dysfunction who present with persistent or worsening bone or muscle symptoms, hypophosphatemia and osteomalacia secondary to proximal renal tubulopathy should be considered

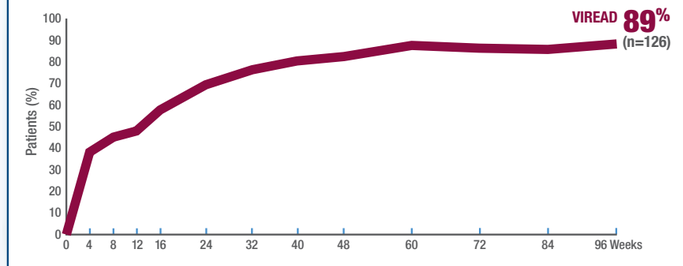
Adverse Reactions

- **In HBV-infected subjects with compensated liver disease:** Most common adverse reaction (all grades) was nausea (9%). Other treatment-emergent adverse reactions reported in >5% of patients treated with VIREAD included: abdominal pain, diarrhea, headache, dizziness, fatigue, nasopharyngitis, back pain, and skin rash

TAKE A CLOSER LOOK AT VIREAD

LAM-resistant VIREAD patients (Study 121)

achieving viral suppression (HBV DNA <400 copies/mL) at 96 weeks of treatment[4,5]



Study 121 was a randomized, double-blind, active-controlled 96-week trial evaluating the safety and efficacy of VIREAD (n=141) compared to an unapproved antiviral regimen (n=139) in subjects with CHB, persistent viremia (HBV DNA ≥1000 IU/mL), and genotypic evidence of LAM resistance. The primary endpoint in Study 121 was HBV DNA <400 copies/mL (69 IU/mL) at Week 96.[4,5]

- As a secondary endpoint, **no HBV resistance (0%)** was detected at **96 weeks** in CHB patients with LAM resistance[4]

Important Safety Information (cont'd)

- **In HBV-infected subjects with decompensated liver disease:** Most common adverse reactions (all grades) reported in ≥10% of patients treated with VIREAD were abdominal pain (22%), nausea (20%), insomnia (18%), pruritus (16%), vomiting (13%), dizziness (13%), and pyrexia (11%)

Drug Interactions

- **Didanosine:** Coadministration increases didanosine concentrations. Use with caution and monitor for evidence of didanosine toxicity (e.g., pancreatitis, neuropathy). Didanosine should be discontinued in patients who develop didanosine-associated adverse reactions. In patients weighing >60 kg, the didanosine dose should be reduced to 250 mg once daily when it is coadministered with VIREAD and in patients weighing <60kg, the didanosine dose should be reduced to 200 mg once daily when coadministered with VIREAD
- **HIV-1 protease inhibitors:** Coadministration decreases atazanavir concentrations and increases tenofovir concentrations; use atazanavir given with ritonavir. Coadministration of VIREAD with atazanavir and ritonavir, darunavir and ritonavir, or lopinavir/ritonavir increases tenofovir concentrations. Monitor for evidence of tenofovir toxicity
- **Drugs affecting renal function:** Coadministration of VIREAD with drugs that reduce renal function or compete for active tubular secretion may increase concentrations of tenofovir

Dosage and Administration

- Recommended dose, in adults and pediatric patients ≥12 years of age (≥35 kg), for the treatment of chronic hepatitis B: one 300 mg tablet, once daily, taken orally, without regard to food
- In the treatment of chronic hepatitis B, the optimal duration of treatment is unknown
- Safety and efficacy in pediatric patients <12 years of age or weighing <35kg with chronic hepatitis B have not been established
- The dosing interval of VIREAD should be adjusted (using recommendations in the table below) and renal function closely monitored in patients with baseline creatinine clearance <50 mL/min

Dosage Adjustment for Patients with Altered Creatinine Clearance

	Creatinine clearance (mL/min)[a]			Hemodialysis patients
	≥50	30-49	10-29	
Recommended 300 mg dosing interval	Every 24 hours	Every 48 hours	Every 72 to 96 hours	Every 7 days or after a total of approximately 12 hours of dialysis[b]

[a]Calculated using ideal (lean) body weight.

[b]Generally once weekly assuming three hemodialysis sessions a week of approximately 4 hours duration. VIREAD should be administered following completion of dialysis.

- The pharmacokinetics of tenofovir have not been evaluated in non-hemodialysis patients with creatinine clearance <10 mL/min; therefore, no dosing recommendation is available for these patients
- No dose adjustment is necessary for patients with mild renal impairment (creatinine clearance 50-80 mL/min). Routine monitoring of estimated creatinine clearance, serum phosphorus, urine glucose, and urine protein should be performed in these patients
- No data are available to make dose recommendations in pediatric patients with renal impairment

Please see Brief Summary of full Prescribing Information, including **BOXED WARNING**, on the adjacent pages.

References: 1. CDC Web site. CDC Features-August 2011: Chronic hepatitis B and Asian & Pacific Islanders. Centers for Disease Control and Prevention. http://www.cdc.gov/Features/ChronicHepatitisB/. Accessed June 26, 2013. **2.** European Association for the Study of the Liver. EASL Clinical Practice Guidelines: Management of chronic hepatitis B virus infection. *J Hepatol.* 2012;57:167-185. **3.** Data on file, Gilead Sciences, Inc. Gilead HBV LAM assessment, IMS MIDAS data. May 2013. **4.** Data on file, Gilead Sciences, Inc. 0121 CSR. **5.** VIREAD Prescribing Information, Foster City, CA: Gilead Sciences, Inc.; October 2013.

300mg tablets®
Viread®
tenofovir disoproxil fumarate

VIREAD® (tenofovir disoproxil fumarate) tablets

Brief summary of full Prescribing Information. Please see full Prescribing Information including Boxed WARNING. Rx only

WARNING: LACTIC ACIDOSIS/SEVERE HEPATOMEGALY WITH STEATOSIS and POST TREATMENT EXACERBATION OF HEPATITIS

- **Lactic acidosis and severe hepatomegaly with steatosis, including fatal cases, have been reported with the use of nucleoside analogs, including VIREAD, in combination with other antiretrovirals *(See Warnings and Precautions)***
- **Severe acute exacerbations of hepatitis have been reported in HBV-infected patients who have discontinued anti-hepatitis B therapy, including VIREAD. Hepatic function should be monitored closely with both clinical and laboratory follow-up for at least several months in patients who discontinue anti-hepatitis B therapy, including VIREAD. If appropriate, resumption of anti-hepatitis B therapy may be warranted *(See Warnings and Precautions)***

INDICATIONS AND USAGE: VIREAD is indicated for the treatment of chronic hepatitis B in adults and pediatric patients 12 years of age and older

The following points should be considered when initiating therapy with VIREAD for the treatment of HBV infection:

- The indication in adults is based on safety and efficacy data from treatment of subjects who were nucleoside-treatment-naïve and subjects who were treatment-experienced with documented resistance to lamivudine. Subjects were adults with HBeAg-positive and HBeAg-negative chronic hepatitis B with compensated liver disease *(See Adverse Reactions)*
- VIREAD was evaluated in a limited number of subjects with chronic hepatitis B and decompensated liver disease *(See Adverse Reactions)*
- The numbers of subjects in clinical trials who had adefovir resistance-associated substitutions at baseline were too small to reach conclusions of efficacy

DOSAGE AND ADMINISTRATION: For the treatment of chronic hepatitis B the recommended dose, in adults and pediatric patients ≥12 years of age (≥35 kg), is one 300 mg tablet, once daily, taken orally, without regard to food. In the treatment of chronic hepatitis B, the optimal duration of treatment is unknown. Safety and efficacy in pediatric patients <12 years of age with chronic hepatitis B weighing <35 kg have not been established. **Dose Adjustment for Renal Impairment in Adults:** Significantly increased drug exposures occurred when VIREAD was administered to subjects with moderate to severe renal impairment. Therefore, the dosing interval of VIREAD tablets 300 mg should be adjusted in patients with baseline creatinine clearance <50 mL/min using the recommendations in Table 1. These dosing interval recommendations are based on modeling of single-dose pharmacokinetic data in non-HIV and non-HBV infected subjects with varying degrees of renal impairment, including end-stage renal disease (ESRD) requiring hemodialysis. The safety and effectiveness of these dosing interval adjustment recommendations have not been clinically evaluated in patients with moderate or severe renal impairment, therefore clinical response to treatment and renal function should be closely monitored in these patients *(See Warnings and Precautions)*. No dose adjustment of VIREAD tablets 300 mg is necessary for patients with mild renal impairment (creatinine clearance 50–80 mL/min). Routine monitoring of estimated creatinine clearance, serum phosphorus, urine glucose and urine protein should be performed in patients with mild renal impairment *(See Warnings and Precautions)*.

Dosage Adjustment for Adult Patients with Altered Creatinine Clearance

	Creatinine clearance (mL/min)[a]			Hemodialysis patients
	≥50	30-49	10-29	
Recommended 300 mg dosing interval	Every 24 hours	Every 48 hours	Every 72 to 96 hours	Every 7 days or after a total of approximately 12 hours of dialysis[b]

a. Calculated using ideal (lean) body weight.
b. Generally once weekly assuming three hemodialysis sessions a week of approximately 4 hours duration. VIREAD should be administered following completion of dialysis.

The pharmacokinetics of tenofovir have not been evaluated in non-hemodialysis patients with creatinine clearance <10 mL/min; therefore, no dosing recommendation is available for these patients. No data are available to make dose recommendations in pediatric patients with renal impairment.

CONTRAINDICATIONS: None.

WARNINGS AND PRECAUTIONS: Lactic Acidosis/Severe Hepatomegaly with Steatosis: Lactic acidosis and severe hepatomegaly with steatosis, including fatal cases, have been reported with the use of nucleoside analogs, including VIREAD, in combination with other antiretrovirals. A majority of these cases have been in women. Obesity and prolonged nucleoside exposure may be risk factors. Particular caution should be exercised when administering nucleoside analogs to any patient with known risk factors for liver disease; however, cases have also been reported in patients with no known risk factors. Treatment with VIREAD should be suspended in any patient who develops clinical or laboratory findings suggestive of lactic acidosis or pronounced hepatotoxicity (which may include hepatomegaly and steatosis even in the absence of marked transaminase elevations). **Exacerbation of Hepatitis after Discontinuation of Treatment:** Discontinuation of anti-HBV therapy, including VIREAD, may be associated with severe acute exacerbations of hepatitis. Patients infected with HBV who discontinue VIREAD should be closely monitored with both clinical and laboratory follow-up for at least several months after stopping treatment. If appropriate, resumption of anti-hepatitis B therapy may be warranted. **New Onset or Worsening Renal Impairment:** Tenofovir is principally eliminated by the kidney. Renal impairment, including cases of acute renal failure and Fanconi syndrome (renal tubular injury with severe hypophosphatemia), has been reported with the use of VIREAD *(See Adverse Reactions)*. It is recommended that estimated creatinine clearance be assessed in all patients prior to initiating therapy and as clinically appropriate during therapy with VIREAD. In patients at risk of renal dysfunction, including patients who have previously experienced renal events while receiving adefovir dipivoxil , it is recommended that estimated creatinine clearance, serum phosphorus, urine glucose, and urine protein be assessed prior to initiation of VIREAD, and periodically during VIREAD therapy. Dosing interval adjustment of VIREAD and close monitoring of renal function are recommended in all patients with creatinine clearance <50 mL/min *(See Dosage and Administration)*. No safety or efficacy data are available in patients with renal impairment who received VIREAD using these dosing guidelines, so the potential benefit of VIREAD therapy should be assessed against the potential risk of renal toxicity. VIREAD should be avoided with concurrent or recent use of a nephrotoxic agent (e.g., high-dose or multiple non-steroidal anti-inflammatory drugs (NSAIDs)) *(See Drug Interactions)*. Cases of acute renal failure after initiation of high dose or multiple NSAIDs have been reported in HIV-infected patients with risk factors for renal dysfunction who appeared stable on tenofovir DF. Some patients required hospitalization and renal replacement therapy. Alternatives to NSAIDs should be considered, if needed, in patients at risk for renal dysfunction. Persistent or worsening bone pain, pain in extremities, fractures and/or muscular pain or weakness may be manifestations of proximal renal tubulopathy and should prompt an evaluation of renal function in at-risk patients. **Coadministration with Other Products:** VIREAD should not be used in combination with the fixed-dose combination products ATRIPLA®, COMPLERA®, STRIBILD® or TRUVADA® since tenofovir disoproxil fumarate is a component of these products. VIREAD should not be administered in combination with adefovir dipivoxil *(See Drug Interactions)*. **Patients Coinfected with HIV-1 and HBV:** Due to the risk of development of HIV-1 resistance, VIREAD should only be used in HIV-1 and HBV coinfected patients as part of an appropriate antiretroviral combination regimen. HIV-1 antibody testing should be offered to all HBV-infected patients before initiating therapy with VIREAD. It is also recommended that all patients with HIV-1 be tested for the presence of chronic hepatitis B before initiating treatment with VIREAD.

Bone Effects

Bone Mineral Density: In clinical trials in HIV-1 infected adults, VIREAD was associated with slightly greater decreases in bone mineral density (BMD) and increases in biochemical markers of bone metabolism, suggesting increased bone turnover relative to comparators. Serum parathyroid hormone levels and 1,25 Vitamin D levels were also higher in subjects receiving VIREAD *(See Adverse Reactions)*.

Clinical trials evaluating VIREAD in pediatric and adolescent subjects were conducted. Under normal circumstances, BMD increases rapidly in pediatric patients. In HIV-1 infected subjects aged 2 years to less than 18 years, bone effects were similar to those observed in adult subjects and suggest increased bone turnover. Total body BMD gain was less in the VIREAD-treated HIV-1 infected pediatric subjects as compared to the control groups. Similar trends were observed in chronic hepatitis B infected adolescent subjects aged 12 years to less than 18 years. In all pediatric trials, skeletal growth (height) appeared to be unaffected *(See Adverse Reactions)*.

The effects of VIREAD-associated changes in BMD and biochemical markers on long-term bone health and future fracture risk are unknown. Assessment of BMD should be considered for adults and pediatric patients who have a history of pathologic bone fracture or other risk factors for osteoporosis or bone loss. Although the effect of supplementation with calcium and vitamin D was not studied, such supplementation may be beneficial for all patients. If bone abnormalities are suspected then appropriate consultation should be obtained.

Mineralization Defects: Cases of osteomalacia associated with proximal renal tubulopathy, manifested as bone pain or pain in extremities and which may contribute to fractures, have been reported in association with the use of VIREAD *(See Adverse Reactions)*. Arthralgias and muscle pain or weakness have also been reported in cases of proximal renal tubulopathy. Hypophosphatemia and osteomalacia secondary to proximal renal tubulopathy should be considered in patients at risk of renal dysfunction who present with persistent or worsening bone or muscle symptoms while receiving products containing tenofovir DF *(See Warnings and Precautions)*.

ADVERSE REACTIONS: Clinical Trials in Adult Subjects with Chronic Hepatitis B and Compensated Liver Disease: *Treatment-Emergent Adverse Reactions:* In controlled clinical trials in subjects with chronic hepatitis B (0102 and 0103), more subjects treated with VIREAD during the 48-week double-blind period experienced nausea: 9% with VIREAD versus 2% with adefovir dipivoxil. Other treatment-emergent adverse reactions reported in >5% of subjects treated with VIREAD included: abdominal pain, diarrhea, headache, dizziness, fatigue, nasopharyngitis, back pain, and skin rash. No significant change in the tolerability profile was observed with continued treatment with VIREAD for up to 240 weeks.

Laboratory Abnormalities: in Studies 0102 and 0103 (0–48 Weeks) laboratory abnormalities (Grades 3–4) reported in ≥1% of subjects treated with Viread (n=426) and adefovir dipivoxil (n=215), respectively, were: any ≥Grade 3 laboratory abnormality (19%, 13%); creatine kinase (M: >990 U/L; F: >845 U/L) (2%, 3%); serum amylase (>175 U/L) (4%, 1%); glycosuria (≥3+) (3%, <1%); AST (M: >180 U/L; F: >170 U/L) (4%, 4%); and ALT (M: >215 U/L; F: >170 U/L) (10%, 6%). Laboratory abnormalities (Grades 3–4) were similar in subjects continuing VIREAD treatment for up to 240 weeks in these trials.

Brief Summary (cont'd)

The overall incidence of on-treatment ALT flares (defined as serum ALT >2 × baseline and >10 × ULN, with or without associated symptoms) was similar between VIREAD (2.6%) and adefovir dipivoxil (2%). ALT flares generally occurred within the first 4-8 weeks of treatment and were accompanied by decreases in HBV DNA levels. No subject had evidence of decompensation. ALT flares typically resolved within 4-8 weeks without changes in study medication. The adverse reactions observed in subjects with chronic hepatitis B and lamivudine resistance who received treatment with VIREAD were consistent with those observed in other hepatitis B clinical trials in adults. *Clinical Trial in Adult Subjects with Chronic Hepatitis B and Decompensated Liver Disease:* In a small randomized, double-blind, active-controlled trial (0108), subjects with CHB and decompensated liver disease received treatment with VIREAD or other antiviral drugs for up to 48 weeks. Among the 45 subjects receiving VIREAD, the most frequently reported treatment-emergent adverse reactions of any severity were abdominal pain (22%), nausea (20%), insomnia (18%), pruritus (16%), vomiting (13%), dizziness (13%), and pyrexia (11%). Two of 45 (4%) subjects died through Week 48 of the trial due to progression of liver disease. Three of 45 (7%) subjects discontinued treatment due to an adverse event. Four of 45 (9%) subjects experienced a confirmed increase in serum creatinine of 0.5 mg/dL (1 subject also had a confirmed serum phosphorus <2 mg/dL through Week 48). Three of these subjects (each of whom had a Child-Pugh score ≥10 and MELD score ≥14 at entry) developed renal failure. Because both VIREAD and decompensated liver disease may have an impact on renal function, the contribution of VIREAD to renal impairment in this population is difficult to ascertain. One of 45 subjects experienced an on-treatment hepatic flare during the 48 week trial.

Clinical Trials in Pediatric Subjects 12 Years of Age and Older with Chronic Hepatitis B: Assessment of adverse reactions is based on one randomized study (0115) in 106 pediatric subjects (12 to less than 18 years of age) infected with chronic hepatitis B receiving treatment with VIREAD (N = 52) or placebo (N = 54) for 72 weeks. The adverse reactions observed in pediatric subjects who received treatment with VIREAD were consistent with those observed in clinical trials of VIREAD in adults. In this study, both the VIREAD and placebo treatment arms experienced an overall increase in mean lumbar spine BMD over 72 weeks, as expected for an adolescent population. The BMD gains from baseline to Week 72 in lumbar spine and total body BMD in VIREAD-treated subjects (+5% and +3%, respectively) were less than the BMD gains observed in placebo-treated subjects (+8% and +5%, respectively). Three subjects in the VIREAD group and two subjects in the placebo group had significant (greater than 4%) lumbar spine BMD loss at Week 72. At baseline, mean BMD Z-scores in subjects randomized to VIREAD were −0.43 for lumbar spine and −0.20 for total body, and mean BMD Z-scores in subjects randomized to placebo were −0.28 for lumbar spine and −0.26 for total body. In subjects receiving VIREAD for 72 weeks, the mean change in BMD Z-score was −0.05 for lumbar spine and −0.15 for total body compared to +0.07 and +0.06, respectively, in subjects receiving placebo. As observed in pediatric studies of HIV-infected patients, skeletal growth (height) appeared to be unaffected *(See Warnings and Precautions)*.

Postmarketing Experience: The following adverse reactions have been identified during postapproval use of VIREAD. Because postmarketing reactions are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to drug exposure: allergic reaction, including angioedema, lactic acidosis, hypokalemia, hypophosphatemia, dyspnea, pancreatitis, increased amylase, abdominal pain, hepatic steatosis, hepatitis, increased liver enzymes (most commonly AST, ALT gamma GT), rash, rhabdomyolysis, osteomalacia (manifested as bone pain and which may contribute to fractures), muscular weakness, myopathy, acute renal failure, renal failure, acute tubular necrosis, Fanconi syndrome, proximal renal tubulopathy, interstitial nephritis (including acute cases), nephrogenic diabetes insipidus, renal insufficiency, increased creatinine, proteinuria, polyuria, asthenia. The following adverse reactions listed above, may occur as a consequence of proximal renal tubulopathy: rhabdomyolysis, osteomalacia, hypokalemia, muscular weakness, myopathy, hypophosphatemia.

DRUG INTERACTIONS: Didanosine: Coadministration of VIREAD and didanosine should be undertaken with caution and patients receiving this combination should be monitored closely for didanosine-associated adverse reactions. Didanosine should be discontinued in patients who develop didanosine-associated adverse reactions. When administered with VIREAD, C_{max} and AUC of didanosine increased significantly. The mechanism of this interaction is unknown. Higher didanosine concentrations could potentiate didanosine-associated adverse reactions, including pancreatitis and neuropathy. Suppression of $CD4^+$ cell counts has been observed in patients receiving VIREAD with didanosine 400 mg daily. In patients weighing >60 kg, the didanosine dose should be reduced to 250 mg once daily when it is coadministered with VIREAD. In patients weighing <60 kg, the didanosine dose should be reduced to 200 mg once daily when it is coadministered with VIREAD. When coadministered, VIREAD and didanosine EC may be taken under fasted conditions or with a light meal (<400 kcal, 20% fat). For additional information on coadministration of VIREAD and didanosine, please refer to the full Prescribing Information for didanosine.

HIV-1 Protease Inhibitors: VIREAD decreases the AUC and C_{min} of atazanavir. Viread should not be coadministered with atazanavir without ritonavir. Lopinavir/ritonavir, atazanavir coadministered with ritonavir, and darunavir coadministered with ritonavir have been shown to increase tenofovir concentrations. Tenofovir disoproxil fumarate is a substrate of P-glycoprotein (Pgp) and breast cancer resistance protein (BCRP) transporters. When tenofovir disoproxil fumarate is co-administered with an inhibitor of these transporters, an increase in absorption may be observed. Patients receiving VIREAD concomitantly with lopinavir/ritonavir, ritonavir-boosted atazanavir, or ritonavir-boosted darunavir should be monitored for VIREAD-associated adverse reactions. VIREAD should be discontinued in patients who develop VIREAD-associated adverse reactions. **Drugs Affecting Renal Function:** Since tenofovir is primarily eliminated by the kidneys, coadministration of VIREAD with drugs that reduce renal function or compete for active tubular secretion may increase serum concentrations of tenofovir and/or increase the concentrations of other renally eliminated drugs. Some examples include, but are not limited to cidofovir, acyclovir, valacyclovir, ganciclovir, valganciclovir, aminoglycosides (e.g., gentamicin), and high-dose or multiple NSAIDs *(See Warnings and Precautions)*. In the treatment of chronic hepatitis B, VIREAD should not be administered in combination with adefovir dipivoxil.

USE IN SPECIFIC POPULATIONS: Pregnancy: *Pregnancy Category B:* There are no adequate and well-controlled studies in pregnant women. Because animal reproduction studies are not always predictive of human response, VIREAD should be used during pregnancy only if clearly needed. *Antiretroviral Pregnancy Registry:* To monitor fetal outcomes of pregnant women exposed to VIREAD, an Antiretroviral Pregnancy Registry has been established. Healthcare providers are encouraged to register patients by calling 1-800-258-4263. *Animal Data:* Reproduction studies have been performed in rats and rabbits at doses up to 14 and 19 times the human dose based on body surface area comparisons and revealed no evidence of impaired fertility or harm to the fetus due to tenofovir. **Nursing Mothers: The Centers for Disease Control and Prevention recommend that HIV-1-infected mothers not breast-feed their infants to avoid risking postnatal transmission of HIV-1.** Samples of breast milk obtained from five HIV-1 infected mothers in the first post-partum week show that tenofovir is secreted in human milk. The impact of this exposure in breastfed infants is unknown. Because of both the potential for HIV-1 transmission and the potential for serious adverse reactions in nursing infants, **mothers should be instructed not to breast-feed if they are receiving VIREAD. Geriatric Use:** Clinical studies of VIREAD did not include sufficient numbers of subjects aged 65 and over to determine whether they respond differently from younger subjects. In general, dose selection for the elderly patient should be cautious, keeping in mind the greater frequency of decreased hepatic, renal, or cardiac function, and of concomitant disease or other drug therapy. **Patients with Impaired Renal Function:** It is recommended that the dosing interval for VIREAD be modified in patients with estimated creatinine clearance <50 mL/min or in patients with ESRD who require dialysis *(See Dosage and Administration)*.

For detailed information, please see full Prescribing Information. To learn more call 1-800-GILEAD-5 (1-800-445-3235) or visit www.VIREAD.com.

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Pablo Figueroa, M.D.

William Ventura, M.D.

napa

Conference Alerts

North America

Keystone Symposia: Integrating Metabolism and Tumor Biology
January 13th to 18th 2015, Vancouver, BC, Canada

Metabolic reprogramming is a hallmark of cancer. Work in recent years has demonstrated extensive interconnectivity between oncogenic signaling pathways and intermediate metabolism. Emerging principles regarding the influence of the tumor microenvironment on cellular metabolism will be discussed in detail, as will new progress toward exploiting metabolic reprogramming to image and treat cancer. The meeting will be partnered with a meeting on PI 3-Kinase Signaling Pathways in Disease, providing a fertile environment for exchange of ideas between these two highly connected fields.
Topics: Tumor metabolism, tumor biology, cancer, cell biology, biochemistry, metabolic diseases
Contact: Attendee Service
Phone: 970-262-1230 or 800-253-0865
Email: info@keystonesymposia.org
http://www.keystonesymposia.org/15J1

Keystone Symposia: Epigenetics and Cancer
January 25th to 30th 2015, Keystone, CO, United States

Cancer epigenetics is a new and rapidly developing area of research. This Keystone Symposia meeting on Epigenetics and Cancer aims to bring together scientists who are interested in understanding the connections between basic epigenetic pathways and the process of cancer. The meeting highlights the mechanisms by which epigenetic pathways control various biological processes and the connections between epigenetic pathways and cancer, thus providing a forum for the interchange of information and knowhow between the two converging fields of cancer research and epigenetics.
Topics: cancer, epigenetics, drug discovery, molecular biology, genetics, genomics, basic mechanisms
Contact: Attendee Services
Phone: 970-262-1230 or 800-253-0865
Email: info@keystonesymposia.org
http://www.keystonesymposia.org/15A4

MISS – 15th Annual Minimally Invasive Surgery Symposiums
February 25th to 28th 2015, Las Vegas, United States

The Annual Minimally Invasive Surgery Symposium (MISS) is the premier meeting of thought leaders in minimally invasive surgery for metabolic/bariatric disorders, hernia, foregut, and diseases of the colon. The conference is led by Executive Director Philip R. Schauer, MD, Cleveland Clinic, along with a faculty of internationally known advanced laparoscopic surgeons and bariatric specialists. In addition to general didactic sessions, the conference will offer optional hands-on workshops in laparoscopic suturing and endoscopic interventions.
Contact: Kathleen Wenzler
Phone: 973-206-8092
Email: k.wenzler@globalacademycme.com
http://www.miss-cme.org

Europe

Advances in radiotherapy for prostate cancer: from theory to practice
December 12th 2014, Cardiff, United Kingdom

This one day meeting will cover recent advances in the radiotherapeutic management of prostate cancer with a particular focus on use of hypofractionated techniques, IMRT and IGRT techniques. The meeting takes a multidisciplinary approach covering topics such as patient preparation, organ motion, and radiotherapy planning techniques to allow you to understand how to put theory into routine clinical practice. Aims and objectives: To develop an understanding of recent advances in radiotherapy for prostate cancer To be able to develop strategies required for the implementation of advanced radiotherapy for prostate cancer To understand the multidisciplinary approach required for the successful radiotherapeutic management for prostate cancer To critically assess the roles of the multidisciplinary team in the development of advanced radiotherapy techniques.
Topics: Prostate, cancer, urology, oncology, radiotherapy
Contact: Rebecca Groves
Phone: 442036682220
Email: Rebecca.groves@bir.org.uk
https://membersarea.bir.org.uk/multievents/displayEvent.asp?Type=Full&Code=5219

GYN – 2015 Progress and Controversies in Gynecologic Oncology Conference
January 16th to 17th 2015, Barcelona, Spain

This meeting will serve as a valuable forum for the presentation and discussion of newly available data across various gynecologic malignancies including ovarian, cervical, and endometrial cancers. Participants will be provided with updates on practice-changing data in a practical and interactive format, fostering discussion, and impacting clinical outcomes for patients.
Topics: Gynecology, radiotherapy, endometrial cancer, ovarian cancer
Phone: +31703067190
Email: gyncongress2015@prIMEoncology.org
http://www.primeoncology.org/live_education/solid_tumor/gyncongress2015.aspx

HPV 2015 – XII International Workshop of Lower Genital Tract Pathology
March 5th to 7th 2015, Rome, Italy

HPV infection and cervical cancer, Cervical cancer screening around the world, HPV vaccination, Challenges in colposcopy, Molecular tests in cytopathology lab, LBC & Automation, Cervical cytopathology : the old and the new, Low genital tract infections and cervical cancer screening, Contraceptives and cervical cancer, The great debates: clinical and pathology perspective, Management of CIN, Issues in colposcopy, Multifocal disease, Classification and quality control in cervical cytopathology, Diagnosis in cytopathology, Legal questions, Training course in colposcopy, Training course in cytopathology, Posters & Communications.
Contact: Organizing Secretariat – triumph C.&C. Srl
Phone: +39 06 35530382
Email: hpv2015rome@thetriumph.com
http://www.hpv2015rome.com

Asia

5th Annual Pharma R&D Asia Congress
January 27th to 28th 2015, Shanghai, China

The 5th Annual Pharma R&D World Asia congress will discuss novel scientific innovations in Discovery and Development in Asia. Topics will cover: global collaboration, changes in the model of CRO outsourcing & partnering strategies, regulation policies and in licensing opportunities. Day 2 topics will also include the latest drug innovation and development activities in improving productivity in Asia. Our esteemed experts will discuss strategies to accelerate drug development timelines.
Topics: Pharma R&D Asia, Pharma R&D, Clinical Trials, Business Development, Drug Development, Drug Discovery, Licensing, Medical Affairs, Outsourcing and Partnering, Regulatory Affairs, Research and Development, Scientific Affairs, Strategic Alliances, Translational Research
Contact: Steph Punfield
Phone: +44 (0) 1865 248455
Email: s.punfield@oxfordglobal.co.uk
http://www.pharmaworldasia-congress.com/download-agenda-marketing/

CARDIORHYTHM 2015
January 30th to February 1st 2015, Hong Kong, China

CardioRhythm 2015 will provide an excellent opportunity for you to stay abreast of the latest developments in the field of cardiac rhythm management. Lectures, case presentations and workshops focusing on sudden cardiac death, new drug and ablation treatment for atrial fibrillation, pacing and ICD advances, cardiac resynchronization techniques, remote patient monitoring, and advances in neuromodulation for heart failure and hypertension will be presented by experts from around the world.
Phone: 852 2911 7921/ 2911 7932
Email: cr2015.secretariat@mci-group.com
http://www.cardiorhythm.com/index/home

BRIEF SUMMARY

ESOMEPRAZOLE STRONTIUM

delayed-release capsules 49.3 mg

For oral use only

Rx Only

BRIEF SUMMARY of Prescribing Information

INDICATIONS AND USAGE

Treatment of GERD in Adults: Esomeprazole strontium is indicated for the short-term treatment (4 to 8 weeks) for healing and symptomatic resolution and maintenance (controlled studies do not extend beyond 6 months) of confirmed erosive esophagitis (EE), the short-term treatment (4 to 8 weeks) of heartburn and other symptoms associated with GERD in adults. **Risk Reduction of NSAID-Associated Gastric Ulcer in Adults, *H. pylori* Eradication to Reduce the Risk of Duodenal Ulcer Recurrence in Adults, and Pathological Hypersecretory Conditions Including Zollinger-Ellison Syndrome in Adults.**

CONTRAINDICATIONS

Esomeprazole strontium is contraindicated in patients with known hypersensitivity to proton pump inhibitors (PPIs). Hypersensitivity reactions, e.g., angioedema and anaphylactic shock, have been reported with esomeprazole use. For information about contraindications of antibacterial agents (clarithromycin and amoxicillin) indicated in combination with esomeprazole strontium, refer to the **CONTRAINDICATIONS** section of their package inserts.

WARNINGS AND PRECAUTIONS

Concurrent Gastric Malignancy: Symptomatic response to therapy with esomeprazole strontium does not preclude the presence of gastric malignancy.

Atrophic Gastritis: Atrophic gastritis has been noted occasionally in gastric corpus biopsies from patients treated long-term with omeprazole, of which esomeprazole is an enantiomer.

***Clostridium difficile* Associated Diarrhea:** Published observational studies suggest that PPI therapy like esomeprazole strontium may be associated with an increased risk of *Clostridium difficile* associated diarrhea. This diagnosis should be considered for diarrhea that does not improve. Patients should use the lowest dose and shortest duration of PPI therapy appropriate to the condition being treated. *Clostridium difficile* associated diarrhea (CDAD) has been reported with use of nearly all antibacterial agents. For more information specific to antibacterial agents (clarithromycin and amoxicillin) indicated for use in combination with esomeprazole strontium, refer to **WARNINGS** and **PRECAUTIONS** sections of those package inserts.

Interaction with Clopidogrel: Avoid concomitant use of esomeprazole strontium with clopidogrel. Clopidogrel is a prodrug. Inhibition of platelet aggregation by clopidogrel is entirely due to an active metabolite. The metabolism of clopidogrel to its active metabolite can be impaired by use with concomitant medications, such as esomeprazole, that inhibit CYP2C19 activity. Concomitant use of clopidogrel with 40 mg esomeprazole reduces the pharmacological activity of clopidogrel. When using esomeprazole strontium, consider alternative anti-platelet therapy.

Bone Fracture: Several published observational studies suggest that PPI therapy may be associated with an increased risk for osteoporosis-related fractures of the hip, wrist, or spine. The risk of fracture was increased in patients who received high-dose, defined as multiple daily doses, and long-term PPI therapy (a year or longer). Patients should use the lowest dose and shortest duration of PPI therapy appropriate to the condition being treated. Patients at risk for osteoporosis-related fractures should be managed according to established treatment guidelines.

Hypomagnesemia: Hypomagnesemia, symptomatic and asymptomatic, has been reported rarely in patients treated with PPIs for at least three months, in most cases after a year of therapy. Serious adverse events include tetany, arrhythmias, and seizures. In most patients, treatment of hypomagnesemia required magnesium replacement and discontinuation of the PPI. For patients expected to be on prolonged treatment or who take PPIs with medications such as digoxin or drugs that may cause hypomagnesemia (e.g., diuretics), health care professionals may consider monitoring magnesium levels prior to initiation of PPI treatment and periodically.

Concomitant Use of esomeprazole strontium with St. John's Wort or Rifampin: Drugs which induce CYP2C19 or CYP3A4 (such as St. John's Wort or rifampin) can substantially decrease esomeprazole concentrations. Avoid concomitant use of esomeprazole strontium with St. John's Wort or rifampin.

Interactions with Diagnostic Investigations for Neuroendocrine Tumors: Serum chromogranin A (CgA) levels increase secondary to drug-induced decreases in gastric acidity. The increased CgA level may cause false positive results in diagnostic investigations for neuroendocrine tumors. Providers should temporarily stop esomeprazole treatment before assessing CgA levels and consider repeating the test if initial CgA levels are high. If serial tests are performed (e.g., for monitoring), the same commercial laboratory should be used for testing, as reference ranges between tests may vary.

Concomitant Use of esomeprazole strontium with Methotrexate: Literature suggests that concomitant use of PPIs with methotrexate (primarily at high dose; see methotrexate prescribing information) may elevate and prolong serum levels of methotrexate and/or its metabolite, possibly leading to methotrexate toxicities. In high-dose methotrexate administration a temporary withdrawal of the PPI may be considered in some patients.

ADVERSE REACTIONS

Clinical Trials Experience

Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared to rates in the clinical trials of another drug and may not reflect the rates observed in practice.

The safety of esomeprazole strontium has been established from adequate and well-controlled studies of esomeprazole magnesium.

Adults: The safety of esomeprazole magnesium was evaluated in over 15,000 patients (aged 18 to 84 years) in clinical trials worldwide including over 8,500 patients in the United States and over 6,500 patients in Europe and Canada. Over 2,900 patients were treated in long-term studies for up to 6-12 months. In general, esomeprazole magnesium was well tolerated in both short and long-term clinical trials.

The safety in the treatment of healing of erosive esophagitis was assessed in 4 randomized comparative clinical trials, which included 1,240 patients on 22.3 mg of esomeprazole magnesium (equivalent to 20 mg of esomeprazole), 2,434 patients on 44.6 mg of esomeprazole magnesium (equivalent to 40 mg of esomeprazole), and 3,008 patients on 20 mg of omeprazole daily. The most frequently occurring adverse reactions (≥1%) in all three groups were headache (5.5%, 5%, and 3.8%, respectively) and diarrhea (no difference among the three groups). Nausea, flatulence, abdominal pain, constipation, and dry mouth occurred at similar rates among patients taking esomeprazole magnesium or omeprazole. Additional adverse reactions that were reported as possibly or probably related to esomeprazole magnesium with an incidence <1% are listed below by body system: **Body as a Whole:** abdomen enlarged, allergic reaction, asthenia, back pain, chest pain, substernal chest pain, facial edema, peripheral edema, hot flushes, fatigue, fever, flu-like disorder, generalized edema, leg edema, malaise, pain, rigors; **Cardiovascular:** flushing, hypertension, tachycardia; **Endocrine:** goiter; **Gastrointestinal:** bowel irregularity, constipation aggravated, dyspepsia, dysphagia, dysplasia GI, epigastric pain, eructation, esophageal disorder, frequent stools, gastroenteritis, GI hemorrhage, GI symptoms not otherwise specified, hiccup, melena, mouth disorder, pharynx disorder, rectal disorder, serum gastrin increased, tongue disorder, tongue edema, ulcerative stomatitis, vomiting; **Hearing:** earache, tinnitus; **Hematologic:** anemia, anemia hypochromic, cervical lymphadenopathy, epistaxis, leukocytosis, leukopenia, thrombocytopenia; **Hepatic:** bilirubinemia, hepatic function abnormal, SGOT increased, SGPT increased; **Metabolic/Nutritional:** glycosuria, hyperuricemia, hyponatremia, increased alkaline phosphatase, thirst, vitamin B12 deficiency, weight increase, weight decrease; **Musculoskeletal:** arthralgia, arthritis aggravated, arthropathy, cramps, fibromyalgia syndrome, hernia, polymyalgia rheumatica; **Nervous System/Psychiatric:** anorexia, apathy, appetite increased, confusion, depression aggravated, dizziness, hypertonia, nervousness, hypoesthesia, impotence, insomnia, migraine, migraine aggravated, paresthesia, sleep disorder, somnolence, tremor, vertigo, visual field defect; **Reproductive:** dysmenorrhea, menstrual disorder, vaginitis; **Respiratory:** asthma aggravated, coughing, dyspnea, larynx edema, pharyngitis, rhinitis, sinusitis; **Skin/Appendages:** acne, angioedema, dermatitis, pruritus, pruritus ani, rash, rash erythematous, rash maculo-papular, skin inflammation, sweating increased, urticaria; **Special Senses:** otitis media, parosmia, taste loss, taste perversion; **Urogenital:** abnormal urine, albuminuria, cystitis, dysuria, fungal infection, hematuria, micturition frequency, moniliasis, genital moniliasis, polyuria; **Visual:** conjunctivitis, vision abnormal.

Endoscopic findings that were reported as adverse reactions include: duodenitis, esophagitis, esophageal stricture, esophageal ulceration, esophageal varices, gastric ulcer, gastritis, hernia, benign polyps or nodules, Barrett's esophagus, and mucosal discoloration.

In two placebo-controlled studies, 710 patients were treated symptomatic GERD and the most common adverse reactions possibly or probably related to esomeprazole magnesium were diarrhea (4.3%), headache (3.8%), and abdominal pain (3.8%). **Combination Treatment with Amoxicillin and Clarithromycin:** In clinical trials using combination therapy with esomeprazole magnesium plus amoxicillin and clarithromycin, no additional adverse reactions specific to these drug combinations were observed. Adverse reactions that occurred were limited to those observed when using esomeprazole magnesium, amoxicillin, or clarithromycin alone. The most frequently reported drug-related adverse reactions for patients who received triple therapy for 10 days were diarrhea (9.2%), taste perversion (6.6%), and abdominal pain (3.7%). No treatment-emergent adverse reactions were observed at higher rates with triple therapy than were observed with esomeprazole magnesium alone. For more information on adverse reactions with amoxicillin or clarithromycin, see their package inserts, refer to **ADVERSE REACTIONS** sections.

Postmarketing Experience

The following adverse reactions have been identified during post-approval use of esomeprazole magnesium. Because these reactions are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to drug exposure. These reports are listed below by body system: **Blood and Lymphatic:** agranulocytosis, pancytopenia; **Eye:** blurred vision; **Gastrointestinal:** pancreatitis, stomatitis, microscopic colitis; **Hepatobiliary:** hepatic failure, hepatitis with or without jaundice; **Immune System:** anaphylactic reaction/shock; **Infections and Infestations:** GI candidiasis; *Clostridium difficile* associated diarrhea; **Metabolism and nutritional disorders:** hypomagnesemia; **Musculoskeletal and Connective Tissue:** muscular weakness, myalgia, bone fracture; **Nervous System:** hepatic encephalopathy, taste disturbance; **Psychiatric:** aggression, agitation, depression, hallucination; **Renal and Urinary:** interstitial nephritis; **Reproductive System and Breast:** gynecomastia; **Respiratory, Thoracic, and Mediastinal:** bronchospasm; **Skin and Subcutaneous Tissue:** alopecia, erythema multiforme, hyperhidrosis, photosensitivity, Stevens-Johnson syndrome, toxic epidermal necrolysis (some fatal).

DRUG INTERACTIONS

Interference with Antiretroviral Therapy: Concomitant use of atazanavir and nelfinavir with PPIs is not recommended. Coadministration of atazanavir with PPIs is expected to substantially decrease atazanavir plasma concentrations and may result in a loss of therapeutic effect and the development of drug resistance. Coadministration of saquinavir with PPIs is expected to increase saquinavir concentrations, which may increase toxicity and require dose reduction. Omeprazole, of which esomeprazole is an enantiomer, has been reported to interact with some antiretroviral drugs. The clinical importance and the mechanisms behind these interactions are not always known. Increased gastric pH during omeprazole treatment may change the absorption of the antiretroviral drug. Other possible interaction mechanisms are via CYP2C19. *Reduced concentrations of atazanavir and nelfinavir:* For some antiretroviral drugs, such as atazanavir and nelfinavir, decreased serum levels have been reported when given together with omeprazole. Following multiple doses of nelfinavir (1250 mg, twice daily) and omeprazole (40 mg daily), AUC was decreased by 36% and 92%, C_{max} by 37% and 89% and C_{min} by 39% and 75%, respectively for nelfinavir and M8. Following multiple doses of atazanavir (400 mg, daily) and omeprazole (40 mg, daily, 2 hr before atazanavir), AUC was decreased by 94%, C_{max} by 96%, and C_{min} by 95%. Concomitant administration with omeprazole and drugs such as atazanavir and nelfinavir is therefore not recommended. *Increased concentrations of saquinavir:* For other antiretroviral drugs, such as saquinavir, elevated serum levels have been reported, with an increase in AUC by 82%, in C_{max} by 75%, and in C_{min} by 106%, following multiple dosing of saquinavir/ritonavir (1000/100 mg) twice daily for 15 days with omeprazole 40 mg daily coadministered days 11 to 15. Clinical and laboratory monitoring for saquinavir toxicity is recommended during concurrent use with esomeprazole. Dose reduction of saquinavir should be considered from the safety perspective for individual patients.

Drugs for Which Gastric pH Can Affect Bioavailability: Esomeprazole inhibits gastric acid secretion. Therefore, esomeprazole may interfere with the absorption of drugs where gastric pH is an important determinant of bioavailability (e.g. ketoconazole, atazanavir, iron salts, and erlotinib can decrease, while the absorption of drugs such as digoxin can increase during treatment with esomeprazole. Concomitant treatment with omeprazole (20 mg daily) and digoxin in healthy subjects increased the bioavailability of digoxin by 10% (30% in two subjects). Esomeprazole is an enantiomer of omeprazole. Coadministration of digoxin with esomeprazole is expected to increase the systemic exposure of digoxin. Patients may need to be monitored when digoxin is taken concomitantly with esomeprazole.

Effects on Hepatic Metabolism/Cytochrome P-450 Pathways: Esomeprazole is extensively metabolized in the liver by CYP2C19 and CYP3A4. *In vitro* and *in vivo* studies have shown that esomeprazole is not likely to inhibit CYPs 1A2, 2A6, 2C9, 2D6, 2E1, and 3A4. No clinically relevant interactions with drugs metabolized by these CYP enzymes would be expected. Drug interaction studies have shown that esomeprazole does not have any clinically significant interactions with phenytoin, quinidine, clarithromycin, or amoxicillin. Although drug interaction studies have not shown that esomeprazole has a clinically significant interaction with warfarin, post-marketing reports of changes in prothrombin measures have been received among patients on concomitant warfarin and esomeprazole therapy. Increases in INR and prothrombin time may lead to abnormal bleeding and even death. Patients treated with PPIs and warfarin concomitantly may need to be monitored for increases in INR and prothrombin time. Esomeprazole may potentially interfere with CYP2C19, the major esomeprazole metabolizing enzyme. Coadministration of esomeprazole 30 mg and diazepam, a CYP2C19 substrate, resulted in a 45% decrease in clearance of diazepam. Clopidogrel is metabolized to its active metabolite in part by CYP2C19. Concomitant use of esomeprazole 40 mg results in reduced plasma concentrations of the active metabolite of clopidogrel and a reduction in platelet inhibition. Avoid concomitant administration of esomeprazole strontium with clopidogrel. When using esomeprazole strontium, consider use of alternative anti-platelet therapy. Omeprazole acts as an inhibitor of CYP2C19. Omeprazole, given in doses of 40 mg daily for one week to 20 healthy subjects in a cross-over study, increased C_{max} and AUC of cilostazol by 18% and 26% respectively. C_{max} and AUC of one of its active metabolites, 3,4-dihydrocilostazol, which has 4-7 times the activity of cilostazol, were increased by 29% and 69% respectively. Coadministration of cilostazol with esomeprazole is expected to increase concentrations of cilostazol and its above mentioned active metabolite. A dose reduction of cilostazol from 100 mg twice daily to 50 mg twice daily should be considered. Concomitant administration of esomeprazole and a combined inhibitor of CYP2C19 and CYP3A4, such as voriconazole, may result in more than doubling of the esomeprazole exposure. Dose adjustment of esomeprazole is not normally required. However, in patients with Zollinger-Ellison's Syndrome, who may require higher doses up to 240 mg/day, dose adjustment may be considered. Drugs known to induce CYP2C19 or CYP3A4 or both (such as rifampin) may lead to decreased esomeprazole serum levels. Omeprazole, of which esomeprazole is an enantiomer, has been reported to interact with St. John's Wort, an inducer of CYP3A4. In a cross-over study in 12 healthy male subjects, St. John's Wort (300 mg three times daily for 14 days) significantly decreased the systemic exposure of omeprazole in CYP2C19 poor metabolisers (C_{max} and AUC decreased by 37.5% and 37.9%, respectively) and extensive metabolisers (C_{max} and AUC decreased by 49.6 % and 43.9%, respectively). Avoid concomitant use of St. John's Wort or rifampin with esomeprazole strontium.

Interactions with Investigations of Neuroendocrine Tumors: Drug-induced decrease in gastric acidity results in enterochromaffin-like cell hyperplasia and increased Chromogranin A levels, which may interfere with investigations for neuroendocrine tumors.

Tacrolimus: Concomitant administration of esomeprazole and tacrolimus may increase the serum levels of tacrolimus.

Combination Therapy with Clarithromycin: Coadministration of esomeprazole, clarithromycin, and amoxicillin has resulted in increases in the plasma levels of esomeprazole and 14-hydroxyclarithromycin. Concomitant administration of clarithromycin with other drugs can lead to serious adverse reactions due to drug interactions [see **WARNINGS** and **PRECAUTIONS** in prescribing information for clarithromycin]. Because of these drug interactions, clarithromycin is contraindicated for coadministration with certain drugs [see **CONTRAINDICATIONS** in prescribing information for clarithromycin].

Methotrexate: Case reports, published population pharmacokinetic studies, and retrospective analyses suggest that concomitant administration of PPIs and methotrexate (primarily at high dose; see methotrexate prescribing information) may elevate and prolong serum levels of methotrexate and/or its metabolite hydroxymethotrexate. However, no formal drug interaction studies of methotrexate with PPIs have been conducted.

SPECIFIC POPULATIONS

Pregnancy: ***Pregnancy Category C:*** There are no adequate and well controlled studies of esomeprazole strontium delayed-release capsules in pregnant women. Teratogenicity was not observed in an embryofetal developmental study in rats with either esomeprazole strontium or esomeprazole magnesium at equimolar oral doses up to 280 mg esomeprazole/kg/day (about 57 times the daily maximum recommended human dose (MRHD) of 40 mg on a body surface area basis). When administered as either the strontium or magnesium salt, changes in bone morphology and physeal dysplasia were observed in pre- and postnatal developmental toxicity studies in rats at doses equal to or greater than 138 mg esomeprazole/kg/day (approximately 33.6 times the daily MRHD of 40 mg on a body surface area basis). Because of the observed effect at the high doses of esomeprazole strontium on developing bone in rat studies, esomeprazole strontium should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

Nursing Mothers: Limited published data indicate that esomeprazole and strontium are present in human milk. Because of the effect of esomeprazole strontium observed at high doses on developing bone in rat studies, a decision should be made whether to discontinue nursing or to discontinue the drug, taking into account the importance of the drug to the mother.

Pediatric Use: The safety and effectiveness of esomeprazole strontium delayed-release capsules have not been established in pediatric patients. Strontium is known to compete with calcium for intestinal absorption and is incorporated into bone. Use in pediatric patients is not recommended because adequate safety studies have not been performed.

Geriatric Use: No overall differences in safety and efficacy were observed between the elderly and younger individuals, and other reported clinical experience has not identified differences in responses between the elderly and younger patients, but greater sensitivity of some older individuals cannot be ruled out.

Use in Patients with Renal Impairment: No dosage adjustment is necessary in patients with mild to moderate renal impairment. The pharmacokinetics and safety of strontium in patients with severe renal impairment has not been studied and, therefore, use in this patient population is not recommended.

OVERDOSAGE

A single oral dose of esomeprazole at 510 mg/kg (about 103 times the human dose on a body surface area basis), was lethal to rats. The major signs of acute toxicity were reduced motor activity, changes in respiratory frequency, tremor, ataxia, and intermittent clonic convulsions. The symptoms described in connection with deliberate esomeprazole overdose (limited experience of doses in excess of 240 mg/day) are transient. Single doses of 80 mg of esomeprazole were uneventful. Reports of overdosage with omeprazole in humans may also be relevant. Doses ranged up to 2,400 mg (120 times the usual recommended clinical dose). Manifestations were variable, but included confusion, drowsiness, blurred vision, tachycardia, nausea, diaphoresis, flushing, headache, dry mouth, and other adverse reactions similar to those seen in normal clinical experience (see omeprazole package insert - **ADVERSE REACTIONS**). No specific antidote for esomeprazole is known. Since esomeprazole is extensively protein bound, it is not expected to be removed by dialysis. In the event of overdosage, treatment should be symptomatic and supportive. As with the management of any overdose, the possibility of multiple drug ingestion should be considered. For current information on treatment of any drug overdose contact a Poison Control Center at 1-800-222-1222.

Please see package insert for full prescribing information.

More detailed information is available upon request.
For more information about esomeprazole strontium contact:
Amneal Pharmaceuticals at 1-877-835-5472.
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September

1. Serotonin deficiency as cause of depression – is it a myth? 9/1/14

A new study in mice suggests that serotonin deficiency may not play as influential a role in depression as has previously been thought. Approach to treating depression is typified by the antidepressant Prozac ever since it was developed. Recent studies show that 60~70% of depressed patients do not respond to Prozac or similar drugs. The researchers developed mice that lacked the ability to produce serotonin and used a variety of test to investigate whether the mice displayed symptoms of depression. The researchers found that the mice showed heightened compulsivity and aggression, but they did not display symptoms of depression. The researchers conclude that serotonin may not be a dominant factor in depression, with risk for the condition being comprised instead of a range of difference factors.
http://www.medicalnewstoday.com/articles/281830.php

2. Are females more susceptible to effects of marijuana? 9/3/14

In the first study to assess sex differences in sensitivities to THC, the key ingredient in cannabis, researchers have found that smoking the concentrated marijuana of today may be riskier for women – thanks to the hormone estrogen. Previous studies have shown that women are more prone to cannabis abuse and dependence than men. In women, cannabis withdrawal symptoms or irritability, sleep disruption and decreased food intake was shown to be more severe, and women also have a higher likelihood of relapsing when quitting the drug. In their study, females developed significantly more tolerance to THC and males were found to be more susceptible to the "munchies effect." Because states like Washington and Colorado have recently legalized recreational marijuana use, the researchers say there is a greater responsibility to understand the differences in cannabis effects on males and females.
http://www.medicalnewstoday.com/articles/281998.php

September

3. FDA approve 'game-changing' drug for advanced melanoma 9/5/14

FDA has granted fast-track approval for a drug called Keytruda (pembrolizumab). This drug was developed by pharmaceutical company Merck & Co. to treat patients with advanced melanoma who are no longer responding to alternative treatment. Clinical trials were tested on more than 600 patients with advanced melanoma who had not responded to previous therapies. In one study, the team treated 173 patients with either 2 milligrams per kilogram (mg/kg) of Keytruda or 10 mg/kg of the drug. The team found that 24% of patients who received the 2 mg/kg dosage of Keytruda experienced tumor shrinkage of more than 30%, while a smaller percentage of patients given the 10 mg/kg dose had tumor shrinkage. The tumors did not regrow in these patients, and the drug's effects remained for at least 1.4-8.5 months, with some patients seeing effects for even longer. The most common side effects were fatigue, cough, nausea, rash, itchy skin, reduced appetite, constipation, diarrhea and joint pain.
http://www.medicalnewstoday.com/articles/282101.php

4. Hourly 5 minute walks 'reverse arterial damage caused by sitting'. 9/8/14

The harm to leg arteries caused by sitting for hours can be easily reversed with hourly 5 minute walks. Sitting for prolonged periods is associated with risk factors for cardiovascular and metabolic disease, such as higher cholesterol levels and greater waist circumference. Because muscles are slackened when sitting, they do not contribute to pumping blood to the heart. This causes blood to pool in the legs, damaging the endothelial function of arteries and impairing blood vessels' ability to expand. The researchers found that, while sitting, the dilation and expansion of the participants' arteries were impaired by up to 50% after just the first hour. Other studies in 2014 have suggested that meetings indirectly benefits work performance in organizations where knowledge-based working is important, and that walking boosts creative thinking.
http://www.medicalnewstoday.com/articles/282194.php

5. Memory loss more common in people with blood type AB 9/10/14

Several research studies have pinpointed lifestyle changes individuals can make to prevent memory loss, such as keeping stress and blood sugars low, and not smoking. But new study pinpoints a potential risk factor for memory loss that we can do nothing about: our blood type. According to the authors of this latest study, led by Dr. Mary Cushman of the University of Vermont College of Medicine in Burlington, the blood type AB is only found in about 4% of the US population, yet people with this blood type were 82% more likely than other types to develop the thinking and memory problems that can lead to dementia. The results show that those with blood type AB made up 6% of the group that developed cognitive impairment, compared with only 4% found in the population.
http://www.medicalnewstoday.com/articles/282051.php

6. Could bee bacteria provide alternatives to antibiotics? 9/10/14

Without pollinators like honeybees, we would have no crop foods. Now, it seems these humble insects may offer another valuable service. As alternative tools against infection in a world that is running out of antibiotics to fight emerging drug-resistant pathogens. Researchers at Lund University in Sweden have discovered that a group of lactic acid bacteria found in the honey stomachs of honeybees has antimicrobial properties - including the ability to fight MRSA and other human bacteria in the lab - and should be investigated as an alternative to antibiotics. They found the lactic acid bacteria were effective against MRSA (methicillin-resistant Staphylococcus aureus), VRE (vancomycin-resistant Enterococcus), Pseudomonas aeruginosa, and other pathogens that cause serious infections in hospital patients and people with weakened immune systems.
http://www.medicalnewstoday.com/articles/282298.php

September

7. Increased Alzheimer's risk linked to long-term benzodiazepine use 9/10/14

Long-term users of benzodiazepines, drugs used to treat anxiety and insomnia, may be at increased risk of developing Alzheimer's disease, according to a new study published in the BMJ. **Previous research has identified an increased risk of dementia among benzodiazepine users, but the mechanism behind the association - as well as the dosage linked to the risk - has not been clear.** The study found that benzodiazepine use for 3 months or more was associated with an increased risk of Alzheimer's disease of up to 51%. Longer the exposure to benzodiazepines, the greater the risk of Alzheimer's. Long-acting benzodiazepines were also found to increase risk more than short-acting benzodiazepines. "It is now crucial to encourage physicians to carefully balance the benefits and risks when initiating or renewing a treatment with benzodiazepines and related products in elderly patients," they add.
http://www.medicalnewstoday.com/articles/282282.php

8. Plant-derived compound 'may effectively treat lupus with fewer side effects' 9/22/14

There is no cure for lupus, but there are medications that can help manage its symptoms. However, some of these drugs cause side effects and increase the risk of other health problems. Now, researchers from the University of Houston, TX, say they have discovered a more natural treatment for the disease that uses a plant extract. So far, it has proved effective and has produced no significant side effects in mice. The researchers found that the compound successfully halted each phase of lupus nephritis development in the mice. "The development of lupus is a two-step reaction," Mohan explains. "First, the immune system develops antibodies that attack the body's own DNA, then that activated immune system attacks the kidneys. We found that CDDO may block both of these steps." If the latter is true, then they say CDDO could pose the same problems as corticosteroids in that it will increase infection risk. However, they note that even if the compound does turn out to be immunosuppressive, it is still likely to produce fewer side effects.
http://www.medicalnewstoday.com/articles/282822.php

9. 1 in 10 antibiotics prescriptions fail, according to new study 9/26/14

The results of a 20 year study published in the BMJ finds that 1 in 10 of all antibiotic prescriptions fail to treat the infection. This marks an increase in the number of antibiotic failures, which is continuing to rise. Over the past 20 years, there has been such a sharp increase in strains of microbes that are resistant to antibiotics that the World Health Organization has declared the issue a global public health crisis. Although many previous studies have assessed antibiotic resistance in hospitals, according to the Cardiff team, experts know "virtually nothing" about the frequency and pattern of antibiotic resistance in primary care. The failure rate of antibiotics that are not normally prescribed as first-line treatments had risen alarmingly. One example of this rise can be observed in the failure rates of trimethoprim, normally used to treat upper respiratory tract infections, which had risen 40% across the treatment period.
http://www.medicalnewstoday.com/articles/283101.php

10. 'Increased risk of venous thromboembolism among NSAID users' 9/25/14

Users of non-steroidal anti-inflammatory drugs are at increased risk of venous thromboembolism, according to a new study published in the journal Rheumatology. Some previous studies have linked increased risk of venous thromboembolism (VTE) - a condition that includes both deep vein thrombosis and pulmonary embolism - with NSAID use, but the evidence has been limited. The researchers compared one cohort study and five case-control observational studies, which included a total of 21,401 VTE events. They found that NSAID users had an overall 1.8-fold increased risk of VTE compared with study participants who did not use NSAIDs.
http://www.medicalnewstoday.com/articles/282961.php

October

11. An ingestible pill with needles could be the new form of injection 10/3/14

Imagine swallowing a pill with tiny needles instead of getting an injection. Then again, imagine swallowing a pill with tiny needles. It may sound painful, but according to the researchers who developed the novel capsule, which could replace painful injections, there are no harmful side effects. "The large size of these biologic drugs makes them nonabsorbable," explains lead author MIT graduate student Carl Schoellhammer. "And before they even would be absorbed, they're degraded in your GI tract by acids and enzymes that just eat up the molecules and make them inactive." The capsules took more than a week to move through the whole digestive tract, and there were no traces of tissue damage, the researchers say. Additionally, the microneedles effectively injected insulin into the lining of the pigs' stomachs, small intestines and colons, which resulted in their blood glucose levels dropping.
http://www.medicalnewstoday.com/articles/283459.php

12. Scientists uncover structure, mechanisms of BRCA2 protein 10/6/14

For the first time, researchers from the UK have created pictures of the BRCA2 protein. Mutations in the gene that encodes this protein are well known to increase the risk of breast and ovarian cancers. Uncovering the structure and mechanisms of the protein may pave the way for treatments targeting BRCA2 gene mutations, according to the investigators. Around 45% of women who have a BRCA2 gene mutation will develop breast cancer by the time they are 70 years old, compared with 12% of women in the general population. While 1.4% of women in the general population will develop ovarian cancer at some point in their lives, this will happen for 11-17% of women with a BRCA2 gene mutation. RAD51 molecules convene on strands of broken DNA with the help of the BRCA2 proteins. The RAD51 molecules then form filaments that look for matching DNA strands that will repair the broken DNA.
http://www.medicalnewstoday.com/articles/283479.php

13. Type 1 diabetes breakthrough as stem cells make billions of human insulin cells 10/10/14

The study is a breakthrough for patients with type 1 diabetes and some with type 2 diabetes, who require daily injections of insulin because they cannot make their own. A new study reveals how scientists successfully created billions of insulin-producing pancreatic beta cells from embryonic stem cells. For their new technique to work in people with type 1 diabetes, the researchers need to add another component that stops a recipient's immune system from attacking the 150 million or so beta cells they would receive. "Furthermore," they note, "these cells secrete human insulin into the serum of mice shortly after transplantation in a glucose-regulated manner, and transplantation of these cells ameliorates hyperglycemia in diabetic mice."
http://www.medicalnewstoday.com/articles/283739.php

14. Could a chemical in broccoli, sprouts help treat autism? 10/14/14

A chemical found in broccoli and other vegetables, sulforaphane, has shown promise for improving some behavioral symptoms of autism. This is according to the results of a small clinical trial led by researchers from Johns Hopkins University School of Medicine and Massachusetts General Hospital for Children. Sulforaphane is a chemical found in a number of vegetables, including broccoli, broccoli sprouts, cabbage, cauliflower and Brussels sprouts. The chemical is most commonly associated with its cancer-fighting properties. The researchers later discovered that sulforaphane can enhance the heat-shock response in the body. This is a series of events that protects cells from damage caused by high temperatures, such as when a person has a fever. For their study, the team enrolled 40 adolescents and young men aged 13-27 who had moderate to severe autism. By 18 weeks, participants who received sulforaphane saw their scores on the Aberrant Behavior Checklist reduce by 34%, while scores on the Social Responsiveness Scale reduced by 17%.
http://www.medicalnewstoday.com/articles/283869.php

15. 3D printing may make individualized medicine more affordable 10/25/14

The latest innovation in medical 3D printing is a 3D printer that could one day make customized medicines on demand. The University of Central Lancashire (UCLan) team says that the machine - which is awaiting a patent application - can "print" a tablet with a precise quantity of medicine that can be taken by a patient. The new technology was made possible by a drug-polymer filament system developed by Dr. Alhnan's team that can replace the original filaments in a 3D printer. This new system allowed the printer to replicate a complex tablet design, matching dose and weight with a high level of accuracy.
http://www.medicalnewstoday.com/articles/284381.php

16. Ibuprofen 'preferable to morphine' for child fractures 10/27/14

The results of a randomized trial published in the CMAJ suggest that ibuprofen is preferable to morphine as a pain reliever for children with broken limbs. Although both drugs provide effective pain relief, ibuprofen is associated with less severe side effects than morphine among this group. The researchers - from London Health Sciences Centre and Western University in Ontario, Canada - compared the outcomes of 66 children whose pain was treated using morphine with the outcomes of 68 children who were administered ibuprofen for fracture pain. All participants were aged 5-17 years. The results demonstrate that, although both of the medications were effective for relieving pain, there were more adverse events - such as drowsiness, nausea and vomiting - associated with morphine. The researchers behind this study found that, after 60 minutes, the ibuprofen group reported the largest decrease in pain intensity. Acetaminophen and codeine did not differ significantly in their ability to reduce pain.
http://www.medicalnewstoday.com/articles/284474.php

17. Stem cells that release cancer-killing toxins offer new brain tumor treatment 10/27/14

Led by Dr. Khalid Shah, a neuroscientist at Harvard Stem Cell Institute, Harvard University, in Cambridge, MA, and also of Massachusetts General Hospital (MGH) in Boston, MA, the scientists found the toxin-releasing stem cells eliminated cancer cells left behind in mouse brains following tumor removal. After doing all of the molecular analysis and imaging to track the inhibition of protein synthesis within brain tumors," says Dr. Shah, "we do see the toxins kill the cancer cells and eventually prolonging the survival in animal models of resected brain tumors." The team now plans to bring together the results of experiments with toxin-releasing stem cells, and the different types of therapeutic stem cells they have developed, to refine their method in mice with glioblastoma, the most common brain tumor in human adults.
http://www.medicalnewstoday.com/articles/284459.php

18. FDA approve first US vaccine for meningococcal disease serogroup B 10/30/14

Neisseria meningitidis can be transmitted from person to person by coughing, kissing or sharing eating utensils. The bacteria infect the bloodstream and the lining surrounding the brain and the spinal cord, causing meningococcal disease. Risk of death or serious long-term problems can be reduced in infected people by treating them with antibiotics, but vaccination is vital for preventing meningococcal disease. The effectiveness of Trumenba was trialled in three randomized studies involving about 2,800 adolescents. After receiving three doses of Trumenba, 82% of the participants had antibodies in their blood that killed four different N. meningitidis serogroup B strains, whereas before vaccination, less than 1% of the participants had these antibodies. Trumenba was also granted "breakthrough therapy" status, which expedites the development and review of medical products to combat life-threatening conditions. Consequently, the FDA was able to evaluate and approve the vaccine's effectiveness in less than 6 months.
http://www.medicalnewstoday.com/articles/284682.php

November

19. A fifth of schizophrenia cases 'may be attributable to T. gondii infection' 11/2/14

The Centers for Disease Control and Prevention (CDC) estimate that around 60 million people in the US may be infected with T. gondii. Infection most commonly occurs through eating undercooked, contaminated meat, drinking contaminated water and coming into contact with cat feces that contain T. gondii. More recently, studies have linked T. gondii infection to schizophrenia, and some have found that antipsychotic medication may even stop the parasite from replicating. But such research has been met with much criticism. In this latest study, Gary Smith, of the School of Veterinary Medicine at the University of Pennsylvania, wanted to gain a better understanding of the link between T. gondii infection and schizophrenia. .
http://www.medicalnewstoday.com/articles/284681.php

20. NSAIDs induce 'suicide' in potentially cancerous intestinal cells 11/4/14

Previous animal studies and clinical trials have shown that nonsteroidal anti-inflammatory drugs (NSAIDs), such as aspirin and ibuprofen, lower the risk of developing intestinal polyps. These polyps can develop into cancer. However, researchers have not previously been able to pinpoint the mechanism by which NSAIDs reduce this cancer risk. The APC mutation makes these genes dysfunctional. Cells affected by the mutation can potentially develop into precancerous polyps and tumors. Although cells that have a mutation in the APC gene are targeted by NSAIDs, healthy cells with the non-mutated gene are unaffected.
http://www.medicalnewstoday.com/articles/284879.php

21. Chagas disease-a new public health threat for Americans? 11/5/14

Researchers from Baylor College of Medicine in Houston, TX, presented the results of their work on 4th November at the 63rd Annual Meeting of the American Society of Tropical Medicine and Hygiene (ASTMH) in New Orleans, LA. They say a large area of the southern US faces a tangible but mostly unrecognized risk of contracting Chagas disease.
http://www.medicalnewstoday.com/articles/284930.php

22. Laundry detergent pods 'pose serious poisoning risk to young children' 11/10/14

Senior author Dr. Gary Smith, director of the Center for Injury Research and Policy at the hospital, and colleagues publish their findings in the journal Pediatrics. Since their introduction into supermarkets in the US in 2010, laundry detergent pods have grown in popularity. Convenience is the main appeal of these products; instead of having to measure out laundry powder, a user can simply pop a pre-measured detergent pod straight into the washing machine. But although laundry detergent pods have their benefits, co-author Dr. Marcel J. Casavant, chief of toxicology at Nationwide Children's Hospital, points out that the products may be appealing to young children.
http://www.medicalnewstoday.com/articles/285177.php

23. CDC: improper contact lens care can lead to blindness 11/14/14

Contact lenses - worn by around 38 million Americans - are a popular alternative to wearing glasses. But improper care of contact lenses can cause eye infections like keratitis, which can lead to blindness. Dr. Jennifer R. Cope, a medical epidemiologist of the National Center for Emerging, Zoonotic and Infectious Diseases at the Centers for Disease Control and Prevention (CDC), and co-author of a new CDC Morbidity and Mortality Weekly Report (MMWR) on keratitis in the US, says: "Contact lenses offer wearers good sight without the hassle of glasses, but they can also make wearers more prone to infection if they're not careful. Users should follow good hygiene and care steps every time they wear, clean and store their contacts to help keep their eyes healthy."
http://www.medicalnewstoday.com/articles/285426.php

24. Habitual running 'may protect against knee osteoarthritis, not cause it' 11/16/14

The research team, co-led by Dr. Grace Hsiao-Wei Lo of Baylor College of Medicine in Houston, TX, recently presented their findings at the American College of Rheumatology Annual Meeting in Boston, MA. Osteoarthritis is a joint disease characterized by the breakdown of the cartilage, joint lining, ligaments and bone. It most commonly affects the knees, hips, hands and spine. Around 26.9 million adults in the US are estimated to have some form of osteoarthritis, with middle-aged and elderly individuals being most affected..
http://www.medicalnewstoday.com/articles/285491.php

25. Just one 10 – second kiss transfers 80 million bacteria 11/17/14

Before germaphobes swear off kissing forever, it should be noted that over 100 trillion microorganisms naturally live in our bodies. Called the microbiome, they are vital for digesting food, synthesizing nutrients and preventing disease. The researchers - led by Remco Kort, of TNO (Netherlands Organization for Applied Scientific Research) and adviser to the Micropia museum of microbes in the Netherlands says that as far as he and his colleagues know, "the exact effects of intimate kissing on the oral microbiota have never been studied. We wanted to find out the extent to which partners share their oral microbiota, and it turns out, the more a couple kiss, the more similar they are."
http://www.medicalnewstoday.com/articles/285563.php

26. Cheap anti-malaria drug shows promise against colorectal cancer 11/19/14

The researchers behind the study - from St George's, University of London in the UK - write about their findings in the journal EBioMedicine. They describe how the drug artesunate - a common anti-malaria medicine - showed a promising effect in slowing tumor cell proliferation in a small group of colorectal cancer patients before they had their tumors surgically removed.
1vhttp://www.medicalnewstoday.com/articles/285691.php

November

27. FDA approve new opioid with abuse-deterrent properties 11/21/14

The new opioid, approved yesterday, is called Hysingla ER (hydrocodone bitartrate), which is an extended-release (ER) opioid analgesic designed to treat pain severe enough to require around-the-clock, long-term treatment. According to the Centers for Disease Control and Prevention (CDC), every day in the US, 114 people die from a drug overdose. Meanwhile, another 6,748 are treated in emergency rooms for the abuse or misuse of drugs. For this reason, the Food and Drug Administration (FDA) deemed it important to protect the public from this growing threat.
http://www.medicalnewstoday.com/articles/285913.php

28. Could yogurt lower the risk of type 2 diabetes? 11/25/14

"We found that higher intake of yogurt is associated with a reduced risk of type 2 diabetes, whereas other dairy foods and consumption of total dairy did not show this association," says senior researcher Dr. Frank Hu. "The consistent findings for yogurt suggest that it can be incorporated into a healthy dietary pattern." Diabetes is a chronic metabolic disease that causes high blood sugar levels. Around 90% of diabetes cases are type 2 diabetes, whereby the body either does not produce enough insulin or suffers from insulin resistance, meaning that the insulin produced is unable to process glucose properly.
http://www.medicalnewstoday.com/articles/285964.php

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